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OPHTHALMOLOGY

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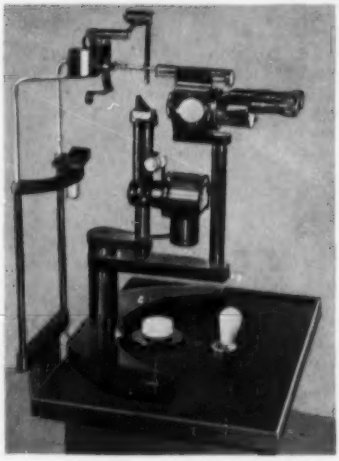

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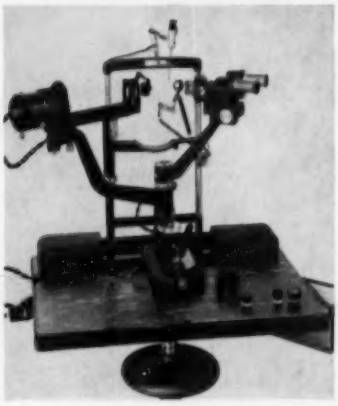

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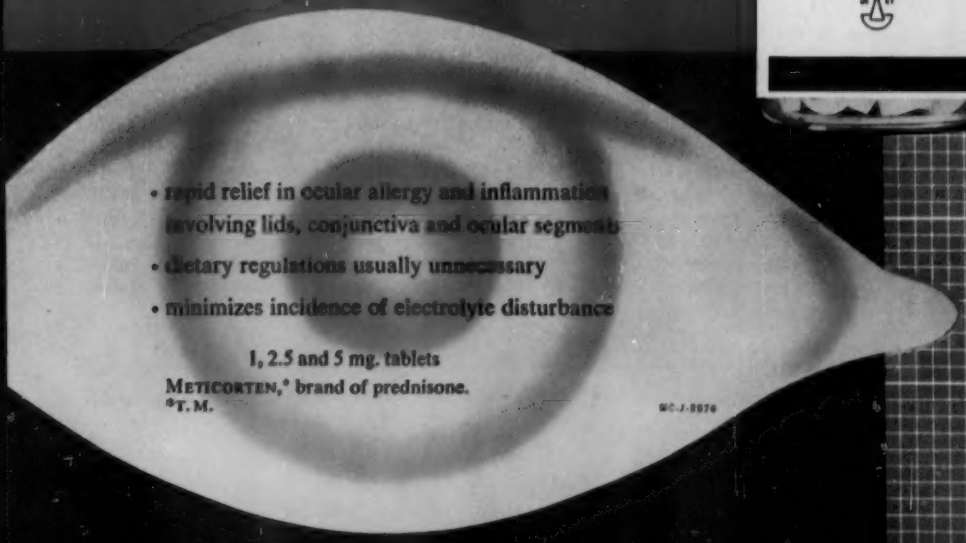

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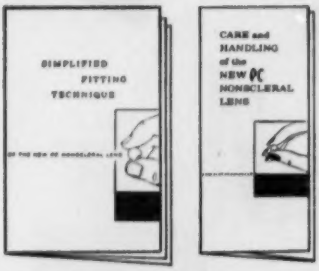

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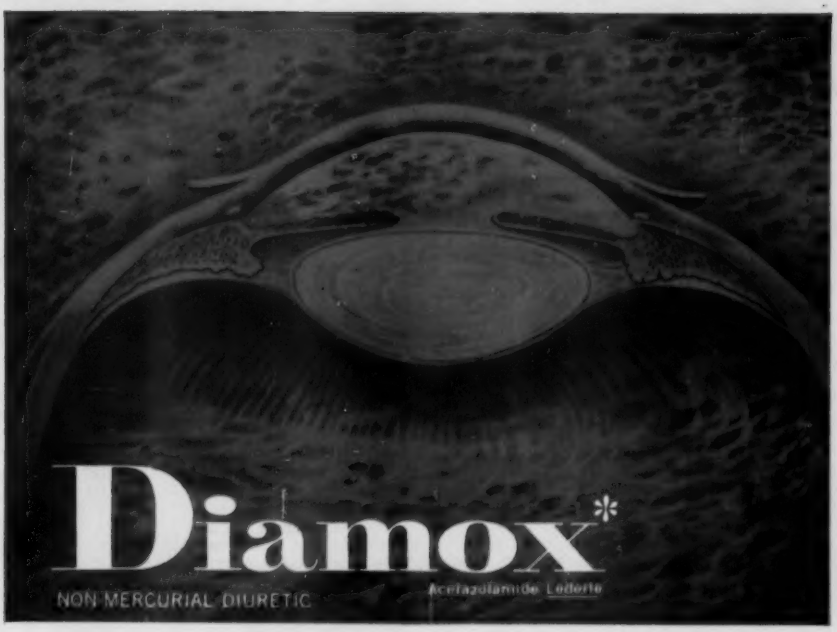

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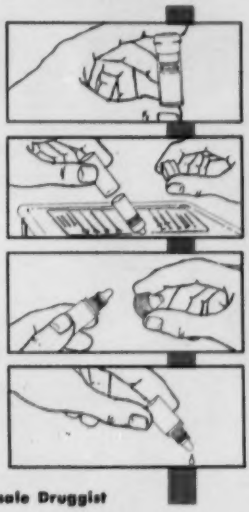

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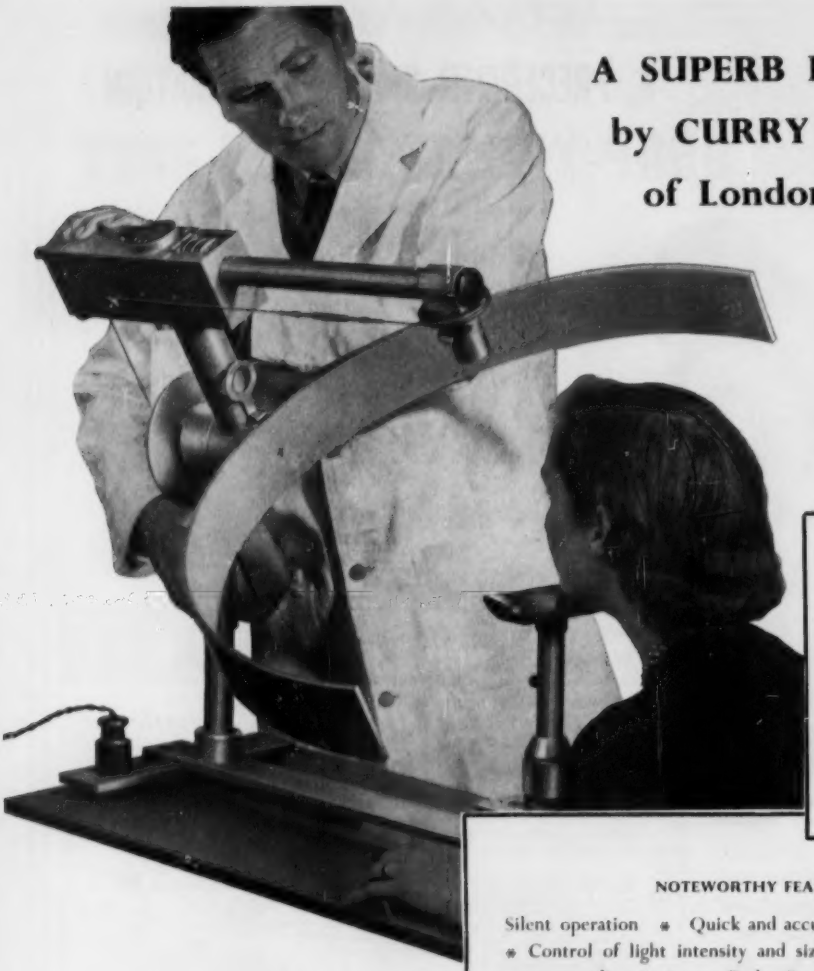

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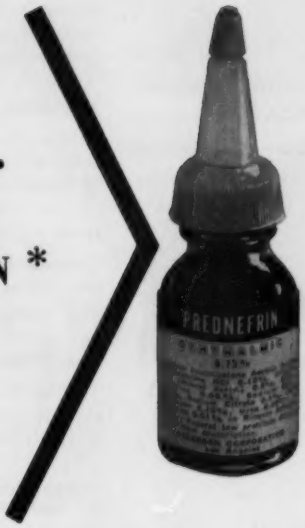

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Chemical Composition of Human Aqueous Humor

Effects of Acetazoleamide

BERNARD BECKER, M.D., St. Louis

Recent experimental approaches to the formation of aqueous humor, its composition, and modifications have relied largely on rabbit studies.[1-3] In this species an aqueous humor is formed which is more alkaline and contains an excess of bicarbonate and a deficit of chloride as compared with plasma. These findings tended to support the Friedenwald-Kinsey theories as to the secretion of aqueous humor. Knowledge of the composition of rabbit aqueous and the reported presence of carbonic anhydrase in the ciliary body[4] led directly to the successful trial of carbonic anhydrase inhibitors, such as acetazoleamide, for suppression of aqueous secretion. In rabbits, tonographic studies revealed that such agents lower intraocular pressure by means of a 50% to 60% suppression of rate of aqueous formation.[5] Furthermore, the alterations in composition of the aqueous humor of posterior and anterior chamber[3] and turnover of test substances[6] are compatible with this degree of inhibition of aqueous flow. Similar effects of carbonic anhydrase inhibition on intraocular pressure and composition of the aqueous humor have been observed in studies with dogs, cats, and guinea pigs. In determinations of changes in aqueous composition it was found that the excess of bicarbonate and deficit of chloride tend to be markedly reduced following acetazoleamide.

In trials on normal or glaucomatous eyes of patients, systemic administration of acetazoleamide was found to lower intraocular pressure without change in tonographic outflow facility.[7,8] Suppression of aqueous secretion was also calculated to be in the range of 50% to 60%. The similarity of results of animal and human studies suggests a role for carbonic anhydrase in the formation of human aqueous humor and a similar mechanism of aqueous secretion. However, differences in the composition of aqueous humor in these two species have been noted. Thus, in 1922, Ascher[9] demonstrated a large excess of chloride in anterior chamber fluids as compared with venous plasma. This was confirmed by Hodgson[10] in 1938 and, more recently, by Remky[11] in 1956. Such findings in the human anterior

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This investigation was supported in part by a research grant, B-621, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service. The research relating to this study was also financed in part under a grant to Washington University School of Medicine made by the Alfred P. Sloan Foundation, Inc. The grant was made upon recommendation of the Council for Research in Glaucoma and Allied Diseases. Neither the Foundation or the Council assumes any responsibility for the published findings of this study.

chamber aqueous are in sharp contrast to the established deficit of chloride in rabbit aqueous. These discrepancies were emphasized recently by Davson and Luck,[12] who reported a deficit of carbon dioxide content in the aqueous humor of one human eye. Therefore it seemed desirable to make a more complete analysis of the chemical composition of individual samples of human anterior chamber aqueous. It is the purpose of this paper to report the results of such a study of the pH, bicarbonate, chloride, and ascorbic concentrations of the aqueous humor from individual eyes as compared with the arterial and venous plasma of the same patient. In addition, the effects of acetazoleamide administration on these constituents were determined.

Methods

Twenty-six patients were selected with senile cataracts of variable degree (vision from "hand motions" to 20/70). These eyes presented no evidence of neoplastic or inflammatory ocular diseases. All demonstrated normal tonograms, open angles to gonioscopy, and full visual fields.

Samples of anterior chamber aqueous were obtained from 22 control eyes and 18 eyes following the systemic administration of acetazoleamide,* (500 mg. every 6 hours for 24 to 28 hours). In 14 patients it was possible to obtain aqueous humor from one eye under the influence of carbonic anhydrase inhibition and from the other eye not subjected to the effects of such treatment. This permitted, in the same patient, a direct comparison of the effects of carbonic anhydrase inhibition on aqueous composition. In 7 of these 14 patients acetazoleamide was administered before tapping the first eye, and in the other 7, before the second eye was punctured. Five to eight days intervened between the procedures on the two eyes.

Blood was obtained from the femoral artery and antecubital vein with use of a heparinized syringe. At the same time, anterior chamber aqueous was drawn into a calibrated pipet within 30 to 60 seconds after retrobulbar injection of 2 cc. of 2% lidocaine hydrochloride in 1:50,000 epinephrine containing 15 TRU of hyaluronidase. The blood samples were drawn or immediately delivered under liquid petrolatum U. S. P. and centrifuged in the cold room. All determinations were carried out on aqueous and plasma within 30 minutes or less of the time of obtaining the specimens. These included determinations of total carbon dioxide content, pH, chloride, and ascorbic acid. Total carbon dioxide content was determined by the method of van Slyke, and bicarbonate was calculated from pH values. Chloride was estimated by the method of Schales, and ascorbic acid was titrated in 4% metaphosphoric acid with dichlorophenolindophenol with use of a 0.1 ml. Gilmont ultramicroburet. The pH was estimated at 37 C colorimetrically for aqueous and plasma and was also checked in each sample of plasma with a Beckman hypodermic type of glass electrode. Methods used were essentially those modifications described by Kinsey.[13] Concentrations are expressed in millimoles per kilogram (mM/kg.) of water. Bicarbonate values for venous plasma were 0.5 to 2.0 (average 1.1 mM.) higher than arterial values. The chloride concentration of venous plasma averaged 1.5 mM. lower than that of arterial plasma. Venous concentrations are omitted from the Tables for the sake of clarity.

Tonography was performed with an electronic tonometer and Leeds and Northrup recorder. Flow rates were calculated with assumption of an episcleral venous pressure of 10 mm. Hg and with use of the 1955 Friedenwald tables.

Results

A. Untreated Patients (Table 1).—In all eyes bicarbonate concentrations in the aqueous humor were lower than those in arterial plasma, with an average deficit of 17%.

* Supplied by Dr. James D. Gallagher, Clinical Research Section, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

TABLE 1.—*Comparison of the Chemical Composition* of Human Aqueous Humor (Untreated) and Arterial Plasma*

Patient	Chloride		Bicarbonate		pH		Ascorbate	
	AC†	Pl†	AC	Pl	AC	Pl	AC	Pl
1	122	114	25.5	28.6			0.58	0.04
2	126	110	22.3	26.3			0.39	0.06
3	122	113	22.1	25.3			0.87	0.07
4	124	117	20.6	23.7			0.47	0.05
5	124	119	22.1	27.3	7.20	7.36	0.81	0.07
6	130	120	19.5	25.8	7.23	7.42	0.89	0.06
7	130	124	19.6	25.4	7.24	7.42	1.33	0.07
8	132	121	21.3	26.9	7.21	7.40	0.51	0.05
9	124	117	20.8	23.5	7.18	7.40	1.43	0.09
10	121	115	21.9	26.8	7.20	7.40	1.03	0.04
11	135	124	17.3	23.6	7.19	7.38	1.64	0.10
12	127	117	18.4	24.9	7.27	7.41	0.15	0.03
13	127	116	20.0	25.8	7.24	7.41	1.21	0.08
14	125	116	21.5	26.1	7.19	7.40	0.37	0.03
19	122	113	22.6	28.0			1.10	0.04
20	123	115	21.8	24.6			1.72	0.08
21	127	117	23.1	26.7			0.75	0.03
22	129	116	22.4	26.2			1.20	0.09
23	125	121	22.3	25.9			1.17	0.07
24	128	117	23.1	28.1	7.19	7.38	1.53	0.10
25	121	113	21.8	24.5	7.20	7.37	0.36	0.04
26	118	113	23.1	27.4	7.23	7.41	0.84	0.06
Mean	126	117	21.5	25.9	7.21	7.40	0.92	0.06
AC/Pl	1.08		0.83		----		15.3	

* All concentrations expressed in millimols per kilogram water (mM/kg. water).
† AC, anterior chamber concentration; Pl, arterial plasma concentration.

Anterior chamber chloride values were found to be higher than in plasma in each eye of this series, with an average excess of 8%. Mean values for bicarbonate were 21.5 mM/kg. for aqueous compared with 25.9 mM/kg. water for arterial plasma. Chloride concentration averaged 126 mM/kg. in the aqueous humor and 117 mM/kg. water in arterial plasma. Thus, a mean deficit of bicarbonate of 4.4 mM/kg. water and an excess of chloride of 9 mM/kg. water were found for these 22 human eyes.

Aqueous humor was found to be more acid than plasma by almost 0.2 pH unit. The average pH of aqueous in these untreated eyes was 7.21, compared with 7.40 for plasma.

Ascorbate concentration in the anterior chamber averaged 0.92 mM/kg. water for these cataractous eyes. This was in consid-

TABLE 2.—*Comparison of the Chemical Composition* of Human Aqueous Humor and Arterial Plasma After Acetazoleamide*

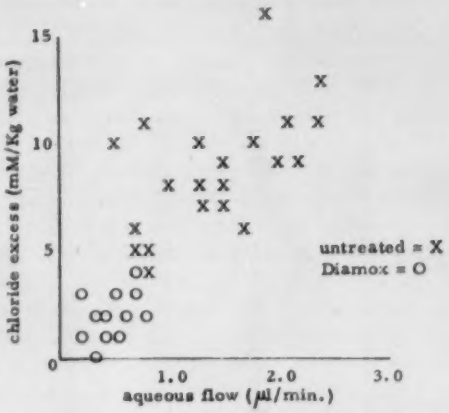
Patient	Chloride		Bicarbonate		pH		Ascorbate	
	AC†	Pl†	AC	Pl	AC	Pl	AC	P
1	124	123	22.8	23.7			0.73	0.04
2	123	119	18.6	19.8			0.64	0.07
3	122	122	17.3	18.2			1.34	0.09
4	124	122	16.8	17.7			0.77	0.06
5	120	121	18.0	19.8	7.18	7.32	1.12	0.06
6	121	118	19.3	21.0	7.21	7.34	1.06	0.06
7	128	127	18.4	20.0	7.23	7.36	1.70	0.07
8	123	120	19.9	22.0	7.24	7.33	0.61	0.05
9	112	109	20.0	20.7	7.25	7.34	1.40	0.08
10	120	119	17.7	18.8	7.18	7.34	0.94	0.05
11	128	127	17.9	19.7	7.20	7.34	1.43	0.06
12	117	115	20.7	21.4	7.27	7.37	0.26	0.02
13	123	122	21.5	22.0	7.28	7.35	1.50	0.07
14	123	121	23.4	25.1	7.20	7.37	0.46	0.04
15	124	120	17.8	20.3	7.23	7.34	1.48	0.05
16	128	125	18.2	19.3	7.30	7.38	0.70	0.05
17	126	125	19.0	19.9	7.25	7.32	1.75	0.09
18	122	121	18.5	19.2	7.22	7.33	1.55	0.07
Mean	123	121	19.2	20.5	7.23	7.35	1.06	0.06
AC/Pl	1.02		0.94		----		17.7	

* All concentrations expressed in millimols per kilogram water (mM/kg. water).
† AC, anterior chamber concentration; Pl, arterial plasma concentration.

erable excess of the mean plasma value of 0.06 mM/kg. water.

B. Acetazoleamide-Treated Patients (Table 2).—In the 18 patients who received acetazoleamide prior to withdrawal of samples, the mean plasma bicarbonate was lowered to 20.5 mM/kg. water and chloride was raised to 121 mM/kg.; aqueous values averaged 19.2 mM/kg. water for bicarbonate and 123 mM/kg. for chloride. Thus, following acetazoleamide the mean bicarbonate deficit in the aqueous humor was only 6% (1.3 mM/kg. water) and the chloride excess was reduced to an average of 2% (2 mM/kg. water). The pH of plasma fell to an average of 7.35 after acetazoleamide, but that of aqueous humor was altered very little and averaged 7.23. The mean difference between aqueous and plasma was thus reduced from 0.19 to 0.12 pH units. Ascorbate concentration in the anterior chamber after acetazoleamide tended to rise to an average of 1.06 mM/kg. water, without significant change in plasma values.

In this series of patients no correlation could be detected between the degree of lens opacity and aqueous humor pH and bicarbonate concentrations or excesses of chloride or ascorbate. However, there was a definite trend for untreated eyes with higher rates of aqueous flow (as measured by tonography) to present greater excesses of chloride in the anterior chamber as compared with plasma concentrations (correlation coefficient=0.62). If the acetazoleamide-treated as well as untreated eyes are included in one plot of chloride excess vs. rate of aqueous flow (Fig.), the correlation of these two variables is even better (correlation coefficient=0.78).



Human aqueous chloride and tonography. Comparison of chloride excess in the anterior chamber (mM/kg. water) and rate of aqueous flow (microliters per minute) in human eyes. Correlation coefficient=0.78; regression equation: chloride excess=4.7×aqueous flow+1.3.

The best statistical evaluation available from these data of the effects of acetazoleamide administration on the composition of human aqueous can be obtained from the comparison of values obtained from the two eyes in the 14 patients where samples were obtained with and without administration of

TABLE 3.—*The Effect of Acetazoleamide on the Chloride Concentration of Human Aqueous Humor*

Patient	Untreated (mM./Kg. Water)			After Acetazoleamide (mM./Kg. Water)		
	AC*	Pl*	AC/Pl*	AC	Pl	AC/Pl
1	122	114	1.07	124	122	1.02
2	126	110	1.15	123	119	1.03
3	122	113	1.08	122	122	1.00
4	124	117	1.06	124	122	1.02
5	124	119	1.04	120	121	0.99
6	130	120	1.08	121	118	1.03
7	130	124	1.05	128	127	1.01
8	132	121	1.09	123	120	1.03
9	124	117	1.06	112	109	1.03
10	121	115	1.05	120	119	1.01
11	135	124	1.09	128	127	1.01
12	127	117	1.09	117	115	1.02
13	127	116	1.10	123	122	1.01
14	125	116	1.08	123	121	1.02
Mean	126	117	1.08	122	120	1.02
S.D.			±0.027			±0.012

* AC, anterior chamber concentration; Pl, arterial plasma concentration; $t_{(n=13)}=7.4$ (untreated vs. acetazoleamide-treated).

TABLE 4.—*The Effect of Acetazoleamide on the HCO_3 Concentration of Human Aqueous Humor*

Patient	Untreated (mM./Kg. Water)			After Acetazoleamide (mM./Kg. Water)		
	AC*	Pl*	AC/Pl*	AC	Pl	AC/Pl
1	25.5	28.6	0.89	22.8	23.7	0.96
2	22.3	26.3	0.85	18.6	19.8	0.94
3	22.1	25.3	0.87	17.3	18.2	0.95
4	20.6	23.7	0.87	16.8	17.7	0.95
5	22.1	27.3	0.81	18.0	19.8	0.91
6	19.5	25.8	0.76	19.3	21.0	0.92
7	19.6	25.4	0.77	18.4	20.0	0.92
8	21.3	26.9	0.79	19.9	22.0	0.91
9	20.8	23.5	0.89	20.0	20.7	0.97
10	21.9	26.8	0.82	17.7	18.8	0.94
11	17.3	23.6	0.73	17.9	19.7	0.91
12	18.4	24.9	0.74	20.7	21.4	0.97
13	20.0	25.8	0.78	21.5	22.0	0.98
14	21.5	26.1	0.82	23.4	25.1	0.93
Mean	20.9	25.7	0.81	19.5	20.7	0.94
S. D.			±0.052			±0.023

* AC, anterior chamber concentration; Pl, arterial plasma concentration; $t_{(AC/Pl)}=8.2$ (untreated vs. acetazoleamide-treated).

carbonic anhydrase inhibitors (Tables 3, 4, 5, and 6). Here it is seen that the bicarbonate deficit in all patients was reduced significantly, from a mean of 81% (S. D. = 5.2%) of plasma untreated to 94% (S. D. = 2.3%) after acetazoleamide. The chloride excess in the anterior chamber was decreased consistently from a mean of 108% (S. D. = 2.7%) of plasma to 102% (S. D. = 1.2%) after acetazoleamide. The pH of aqueous humor was not significantly altered in spite of the consistent decrease in plasma pH. Thus, the mean pH difference between anterior chamber and plasma was decreased from 0.19 (S. D. = 0.021) to 0.13 (S. D. = 0.32) pH units. These induced changes in chloride, bicarbonate, and pH discrepancies from plasma are statistically significant. Ascorbate concentration in the anterior chamber rose in 12 of the 14 patients without significant change in plasma values. Average values for the 14 patients were 13.5 (S. D. = 4.7) times plasma concentration untreated and 16.6 (S. D. = 4.6) times plasma level following acetazoleamide. The alteration in ascorbate concentration after acetazoleamide is not statistically significant, however (1.7 times the standard error of the means).

Comment

The results of the present study confirm the findings of previous investigators of a considerable excess of chloride in the anterior chamber of human eyes and amplify the suggestion of Davson and Luck [12] of a deficit of bicarbonate. The lower pH found in the aqueous humor of human eyes is consistent with these findings. The ascorbate excess found in the aqueous of all human eyes studied agrees well with previous reports.[14,15] The present values for chloride

TABLE 5.—*The Effect of Acetazoleamide on the pH of Human Aqueous Humor*

Patient	Untreated			After Acetazoleamide		
	AC*	Pl*	AC—Pl*	AC	Pl	AC—Pl
5	7.20	7.38	−0.18	7.18	7.32	−0.14
6	7.23	7.42	−0.19	7.21	7.34	−0.13
7	7.24	7.42	−0.18	7.23	7.36	−0.13
8	7.21	7.40	−0.19	7.24	7.33	−0.09
9	7.18	7.40	−0.22	7.25	7.34	−0.09
10	7.20	7.40	−0.20	7.18	7.34	−0.16
11	7.19	7.38	−0.19	7.20	7.34	−0.14
12	7.27	7.41	−0.14	7.27	7.37	−0.10
13	7.24	7.41	−0.17	7.28	7.35	−0.07
14	7.19	7.40	−0.21	7.20	7.37	−0.17
Mean	7.21	7.40	−0.19	7.22	7.35	−0.13
S. D.			±0.021			±0.032

* AC, anterior chamber value; Pl, arterial plasma value; AC—Pl, pH difference; $t_{(AC/Pl)}=4.6$ (untreated vs. acetazoleamide-treated).

TABLE 6.—*The Effect of Acetazoleamide on the Ascorbic Concentration of Human Aqueous Humor*

Patient	Untreated (mM./Kg. Water)			After Acetazoleamide (mM./Kg. Water)		
	AC*	Pl*	AC/Pl*	AC	Pl	AC/Pl
1	0.58	0.04	14.5	0.73	0.04	18.3
2	0.39	0.06	6.5	0.64	0.07	9.1
3	0.87	0.07	12.4	1.34	0.09	14.9
4	0.47	0.05	9.4	0.77	0.06	12.8
5	0.81	0.07	11.6	1.12	0.06	18.7
6	0.89	0.06	14.8	1.06	0.06	17.7
7	1.33	0.07	19.0	1.70	0.07	24.3
8	0.51	0.05	10.2	0.61	0.05	12.2
9	1.43	0.09	15.9	1.49	0.08	16.1
10	1.06	0.04	25.8	0.94	0.05	18.8
11	1.64	0.10	16.4	1.43	0.06	23.8
12	0.15	0.03	5.0	0.26	0.02	13.0
13	1.21	0.08	15.1	1.50	0.07	21.4
14	0.37	0.03	12.3	0.46	0.04	11.5
Mean	0.83	0.06	13.5	1.00	0.06	16.6
S. D.			±4.7			±4.6

* AC, anterior chamber concentration; Pl, arterial plasma concentration; $t_{(AC/Pl)}=1.7$ (untreated vs. acetazoleamide-treated).

(8% excess over plasma) and bicarbonate (17% deficit) in untreated human eyes resemble the data for monkey eyes (9% excess of chloride and 23% deficit of bicarbonate as compared with arterial plasma) and for the cerebrospinal fluids of man, monkey, dog, cat, guinea pig, and rabbit.[16]

However, the composition of human and monkey aqueous humor is in sharp contrast to values for rabbit and guinea pig eyes.[1,3,17] Thus, rabbit anterior chamber aqueous humor demonstrates an average bicarbonate excess over arterial plasma of 35% (8.4 mM/kg. water) and guinea pig aqueous has a 45% excess (10.6 mM/kg. water). The mean deficit of chloride in the rabbit anterior chamber is 7% (8.0 mM/kg. water), and in guinea pigs it is 10% (12 mM/kg. water). Furthermore, rabbit and guinea pig aqueous are more alkaline than arterial plasma by 0.10 to 0.15 pH units. However, guinea pig, rabbit, and human eyes all have in common a considerable excess concentration of ascorbate compared with plasma values.

In spite of their differences in composition, rabbit and human eyes respond to carbonic anhydrase inhibition with a decrease in the discrepancies from plasma in concentrations of chloride and bicarbonate. This is consistent with the tonographic evidence for a decreased rate of aqueous secretion in both species after acetazoleamide. Thus, in the rabbit the mean excess of bicarbonate is reduced from 35% (8.4 mM.) to 10% (2.2 mM.) and deficit of chloride is reduced from 7% (8.0 mM.) to 4% (5.0 mM.). In human eyes the mean excess of chloride is reduced from 8% (9.0 mM.) to 2% (2.0 mM.) and deficit of bicarbonate is reduced from 19% (4.8 mM.) to 6% (1.2 mM.) after acetazoleamide. In both species ascorbate concentrations in the aqueous humor tend to rise after carbonic anhydrase inhibition, suggesting a smaller effect on ascorbate secretion than on the transfer of water.

The findings in human eyes fail to support the primary role attributed by Friedenwald and Kinsey to bicarbonate in the formation of aqueous humor, at least in primate eyes. The intriguing possibility of the secretion of hydrogen ions in these eyes is suggested by the low pH and excess of chloride in human aqueous. Although the decreased pH and bicarbonate deficit may result in part from lactate production in the eye, this would not explain the chloride excess. The relationship of chloride excess in human aqueous to the rate of flow provides suggestive evidence for a primary role of the secretion of this anion in primate eyes. However, this conclusion cannot be drawn in the absence of posterior chamber data. Thus, if the posterior chamber concentration of chloride were constant the anterior chamber value would vary with rate of flow

because of time available in the anterior chamber for diffusional loss. The secretion of sodium by the ciliary epithelium remains a reasonable possibility, but it fails to explain the excess of chloride in some species and of bicarbonate in others. The thesis of Davson [16] of variable needs for bicarbonate buffering capacity in different-sized eyes provides entertaining teleologic speculation but does not resolve the problem of the mechanism of specificity of anions secreted.

The role of the enzyme carbonic anhydrase in these secretory processes remains unexplained. It may provide the bicarbonate buffering capacity needed by the secretory cell of the ciliary body, as postulated for the gastric mucosa and the renal tubule.[18] This hypothetical role could hold for variety of secretory mechanisms implicating the transfer of cations or anions or both as primary secretory products. It would account for the finding that carbonic anhydrase inhibition by acetazoleamide administration appears to result in a partial suppression of such different secretory activities as the reabsorption of bicarbonate in the renal tubule and the formation of pancreatic secretion, gastric hydrochloric acid, cerebrospinal fluids, and the different aqueous humors of various species.

Summary

The anterior chamber aqueous humor of 22 cataractous human eyes was found to be more acid (by an average of 0.19 pH units) and to contain an 8% mean excess of chloride (9.0 mM/kg. water), a 17% mean deficit of bicarbonate (4.4 mM/kg. water), and a fifteenfold average excess of ascorbate (0.86 mM/kg. water) as compared with arterial plasma of the same patients.

The chloride excess in the anterior chamber tended to correlate with the rate of aqueous flow as measured by tonography.

These results contrast with the alkaline aqueous of the rabbit eye, which contains a deficit of chloride and an excess of bicarbonate and ascorbate with reference to plasma values.

In both species, however, the systemic administration of acetazoleamide decreases significantly the discrepancies from plasma concentrations of chloride and bicarbonate but tends to increase the ascorbate excess.

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Variations of the Fundus Reflex in Ametropia

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In direct ophthalmoscopy, before the fundus is examined with the instrument held close to the subject's eye, it is customary to observe the fundus reflex in the pupillary area for opacities in the media, especially the lens. This is done at a distance of 12 in. (300 mm.) or so. However, with the modern electric ophthalmoscope, even when there are no intervening opacities in the media the fundus reflex almost never is uniform in brightness. One portion of the pupillary area usually is much brighter than the remainder, and the boundary between these two areas is a curved one with the concavity upward. The position and extent of these two areas, the brighter area and the darker area, vary with the refractive state of the eye. The description and explanation of this phenomenon will be attempted in general terms. Although rough numerical examples will be worked out, chiefly to clarify the explanation, it will become apparent that many variables are involved and that certain approximate assumptions have to be made.* Therefore the descriptions and explanations must be regarded only as crude approximations, qualitative rather than quantitative.

The Modern Electric Hand Ophthalmoscope

Illuminating Mechanism.—Modern electric hand ophthalmoscopes use either a May-type prism or a plane mirror to reflect forward the upright emerging light.

The source of light is a tiny luminous coiled filament. Behind the filament, at a distance slightly greater than its focal length, is a sharply curved planoconvex condensing lens almost hemispheric in shape. This lens converges the rays that radiate toward it from the luminous filament, thereby transmitting a more concentrated beam of light. Directly behind the condenser is a diaphragm that can be rotated so as to center any one of two or more different-sized circular apertures with the condenser. Any one of these openings when in place will be the aperture stop of the system, as the largest opening is smaller in diameter than either the condenser lens mount or the projecting lens farther on (Fig. 1). Following the condenser aperture is an air space of variable length, depending on the make of the instrument.

After the beam of emerging light passes through the condenser and the air space, it is given additional convergence. In the mirror ophthalmoscopes this is accomplished by one or more converging lenses called projecting lenses. Then, on emergence from the instrument's head, the beam is reflected forward (horizontally) by the plane mirror. In the prism ophthalmoscopes the lower surface of the prism has a convex curvature and acts as a projecting lens. The prism has two reflecting surfaces, its front and rear surfaces. The beam, after entering the prism through its lens surface, first strikes the oblique anterior surface at a small angle and undergoes total internal reflection. Then it strikes the slabbed-off, silvered, upper part of the rear surface of the prism at a high angle and undergoes plane-mirror reflection forward. On emerging through the upper part of the oblique anterior surface of the prism (the "face" of the prism), the beam undergoes a slight prismatic deviation which gives it a horizontal direction.

An enlarged inverted image of the filament, magnified as much as four times in

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* All values assumed for the standard eye and all formulas used for the computations are those that are given by Duke-Elder.[1]

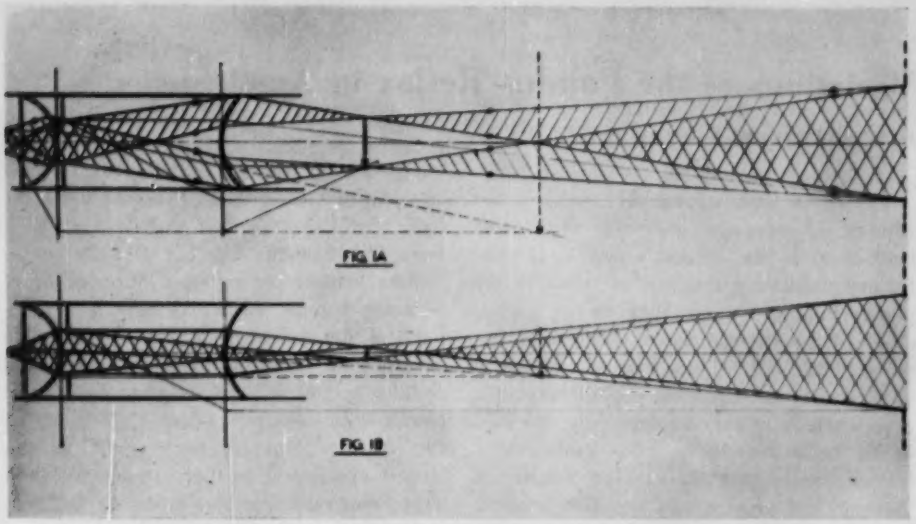


Fig. 1.—Schematic graphic constructions which illustrate the optical mechanisms used in the illuminating system of the ordinary electric hand ophthalmoscope. The sectional paths of bundles of light rays emanating from the extremities of the length and breadth of the filament are shown by cross hatched lines. *A* represents a longitudinal cross section in the plane through the length of the filament, the arrow representing the filament in its longest dimension. *B* represents a section in the transverse plane at right angles to the plane of *A*. The arrow represents the width of the filament.

The filament or light source is located just in front of the principal focal point of the sharply curved planoconvex condensing lens. Immediately behind the condenser is a circular aperture. This is followed by an air space, at the end of which is the refracting surface of the prism. In ophthalmoscopes that use a plane reflecting mirror instead of a May-type prism this would be a separate lens. The two reflections that the light rays undergo inside the prism are not shown, since the vergence of the light rays is not affected thereby.

The construction lines necessary for determining the position and size of the images of the filament and of the aperture are shown as faint thin lines. The posterior principal focal point of the condenser and the anterior principal focal point of the lens surface of the prism have been made to coincide. The principal focal planes of both lenses also are shown.

The condenser and the lens surface of the prism jointly focus the light from the filament to form a real inverted magnified image of the filament in the front face of the prism (or in the mirror, whenever a prism is not used). This image of the filament is the immediate light source for an examined eye. The lens surface of the prism (or the projecting lens) forms a real inverted magnified image of the aperture opening which is located out in space, in front of the ophthalmoscope. All rays which pass through the aperture necessarily pass through corresponding points in the image of the aperture.

some instruments, is formed by the combined refractions of the condensing and projecting lenses, either at the front surface of the prism, or in the plane mirror, about 1.0 mm. from the top edge. A magnified inverted image of the aperture behind the condenser is formed by the projecting lens and is located out in space in front of either the mirror or the prism face. This circular image has a size that ranges from 4 to 12 mm. in diameter, depending on the size of the aperture and the make of the instrument, and it is located anywhere from 3 to 12 cm., or more, in front of the instrument. This image is the exit pupil of the system. All rays which pass through the condenser aperture must pass through corresponding points in the magnified inverted image of the aperture.

The electric hand ophthalmoscope has been designed for direct ophthalmoscopy at a distance of about 2.5 cm. from the cornea of an observed eye. At this close distance an image of the filament cannot be formed on the retina of an observed eye because the latter is too close to the face of the prism.

If the retina were very much farther back —about 66 mm. behind the corneal vertex— then an outline or image of the filament on the retina would be visible to the observer. Thus, when the ophthalmoscope is used at 2.5 cm. or less from an eye the retina intercepts the converging beam of light, which has been refracted by the cornea and the lens, long before it can reach a focus.

Retinal Illumination by a Source at Twelve Inches.—The immediate source of light for an examined eye is the image of the luminous filament that is formed in the face of the prism, or mirror, of the ophthalmoscope. The size of the bounding envelope of this image varies considerably in instruments of different manufacture. It will not be amiss to assume a size of 3.0×1.2 mm. as an average. Such a source of light at 12 in. (approximately 300 mm.) from the cornea will tend to come to a focus, in a standard nonaccommodating eye of 58.6 D. of refracting power, at a distance of 25.7 mm. behind the corneal vertex.† However, this image will be located on the retina of an unaccommodated eye only under one very special and unlikely circum-

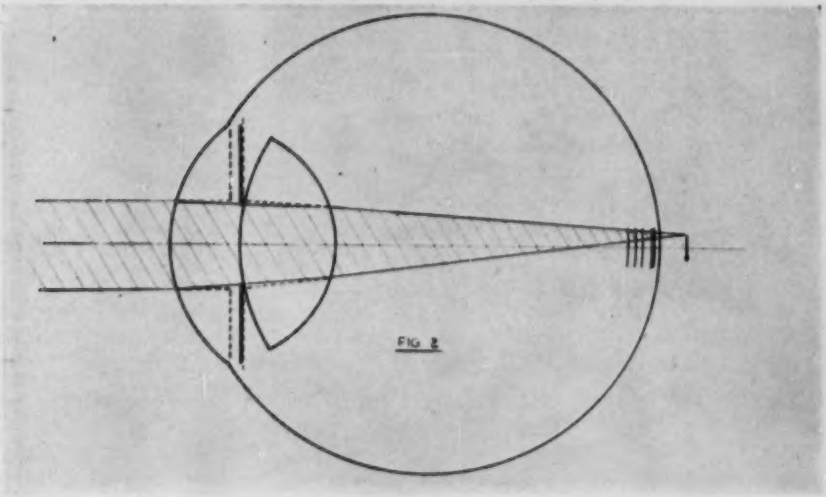
† Computed by using the formula $\frac{f_1}{u} + \frac{f_2}{v} = 1$ where f_1 is the anterior focal length of the eye; f_2 the posterior focal length; u and v the object and image distances, respectively, from the principal planes of the eye.

Fig. 2.—An enlarged schematic vertical (sagittal) cross section of a standard eye is depicted; also, the image which tends to be formed of the width of the filament in the face of the prism, 300 mm. from the corneal vertex, is shown. The drawing is approximately to scale except for the image. This has been drawn about 20 times larger than it should be, because of the mechanical difficulty of drawing such a tiny object.

Actually, no focused image is formed as has been drawn, because the retina intercepts the light bundles before they can reach a focus. The position of the retina in various amounts of hypermetropia (starting with 0.5 *D.* and going through 1.0, 2.0, 3.0, 4.0 *D.*, from behind forward) is indicated by the parallel lines in front of the retina.

The entrance and exit pupils of the eye are indicated by interrupted lines. The path of the bundle of light rays which converges to one extremity of the image is indicated. It enters the eye as if to fill the entrance pupil. Then, after refraction by the cornea, it converges to pass through the circular pupillary aperture. After refraction by the two lens surfaces it leaves the lens as if it had emerged through the exit pupil. (The entrance pupil is the enlarged, virtual, and erect image of the true pupil as formed by the cornea. The exit pupil is the enlarged, virtual, and erect image of the true pupil as formed by the posterior surface of the lens).

It is obvious that the size of the illuminated retinal area which is intercepted increases with the amount of hypermetropia. It also is obvious that the width of the cone of light which enters the eye varies directly with the size of the pupillary aperture.



stance, namely, if the eye is myopic by the exact amount necessary to make its far point coincide with the location of the ophthalmoscopic light source—about 3.3 D. for a distance of 300 mm. from the corneal vertex. In all other refractive conditions in unaccommodated eyes the retina will be illuminated by out-of-focus rays proceeding either to or from the place of focus. The illuminated retinal area will be larger than the image by an amount that will depend partly on the size of the pupil and partly on the location of the retina (Fig. 2).

Hypermetropia

The Illuminated Retinal Area in Hypermetropia.—The far point of an eye is that point on the axis from which a distinct image is formed on the retina while the eye is not accommodating. In hypermetropia the far point is virtual, being situated behind the retina. Thus, in hypermetropia with a principal point refraction of 0.5 D. the far point is located at 1/0.5 meters, or 2000 mm. behind the second principal point of the eye. Likewise, for 1.0, 2.0, 3.0 and 4.0 D. of hypermetropia the far points are at 1000, 500, 333, and 250 mm., respectively, behind the second principal plane.

In hypermetropia the retina will intercept the refracted rays from the ophthalmoscope before they can reach a focus. Assuming that the hypermetropia is axial, the location of the retina for various amounts of hypermetropia can be computed from the general formula for object and image distances because the retina and the far point are in conjugate focal relationship and the location of the far point is established by the amount of hypermetropia that is assumed to be present. Therefore, for hypermetropias of 0.5, 1.0, 2.0, 3.0, and 4.0 D. the retinas will be located at the distances of 22.6, 22.4, 22.0, 21.7, and 21.3 mm., respectively, behind the posterior focal plane. Then, from a construction such as Figure 2 and the use of the proportional relationships of homologous parts of similar triangles, it is easy to determine the sizes of the illuminated retinal areas for various amounts of hypermetropia, assuming the pupils of these eyes all to be 4 mm. in diameter, and the exit pupils all to be 4.2 mm. in diameter and 0.1 mm. behind the actual pupillary aperture. The image of the 3.0×1.2 mm. light source in the face of the prism at 300 mm. from the cornea will be 0.18×0.07 mm. in size.‡ For hypermetropias of 0.5, 1.0, 2.0, 3.0, and 4.0 D. the illuminated retinal areas, approximately elliptical in shape, will have sizes of 0.45×0.35, 0.49×0.39, 0.56×0.46, 0.62×0.52, and 0.69×0.59 mm., respectively, corresponding to the major and minor axes of the ellipses, the major axis being horizontal and the minor axis being vertical.

The Return Light from Hypermetropic Eyes.—The elliptical illuminated retinal area —long axis horizontal because that is the position of the filament image in the face of the prism or mirror of the ophthalmoscope—that is intercepted before the entering cone of light can reach a focus becomes a secondary source of illumination because it reflects light diffusely rather than specularly. Each point in the illuminated area emits light in all directions. Only a part of that portion of the emitted light which emerges through the pupil is capable of being intercepted at any one moment by the observer's eye behind the sight hole of the ophthalmoscope. The cone of emergent light that issues through the pupil is very much larger in diameter at 12 in. in front of the eye than either the sight hole or the observer's pupil. The vergence of this emerging light varies with the refractive condition of the examined eye.

In hypermetropia the rays issuing from an examined eye will be divergent, as if coming from an enlarged erect virtual image of the illuminated retinal area located behind

‡ The size of an image formed by the dioptric apparatus of the eye may be computed from the formula $\frac{o}{i} = \frac{f_1 - u}{\quad}$, where f_1 is the anterior focal length; u, the distance between the object and the first principal plane, and o and i, the object and image sizes.

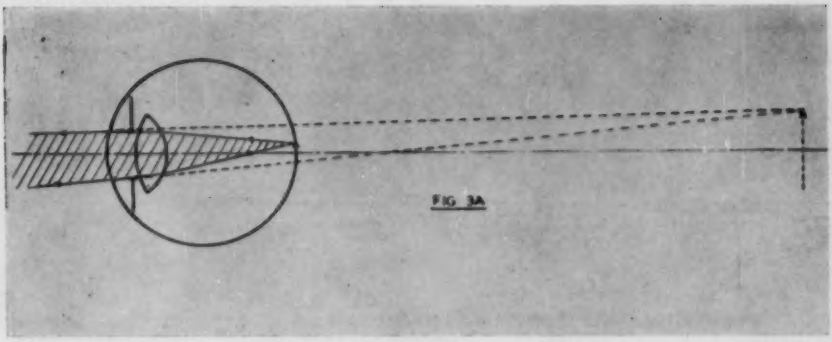


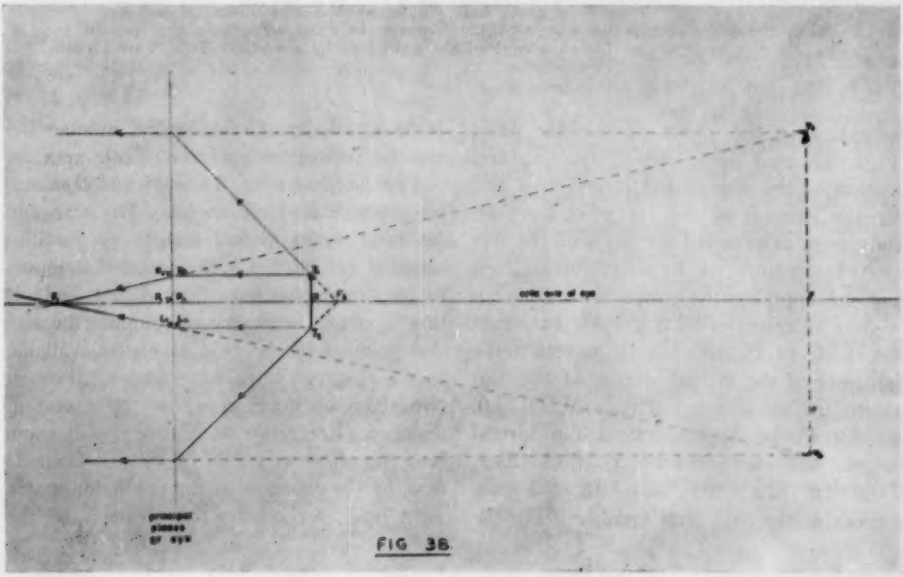
Fig. 3A.—The emergence of light rays from a hypermetropic eye is shown schematically and in cross section. The arrow on the retina represents the illuminated retinal area that is formed by interception of the cone of refracted light entering the eye from the ophthalmoscope. The bundle of rays that emerges from one extremity of the illuminated retinal area is shown.

It will be seen that the emerging rays of light, after refraction first by the lens and then by the cornea, still are slightly divergent and appear to come from an enlarged erect virtual image of the illuminated retinal area that is situated behind the retina in the plane of the far point of the eye.

The drawing is not to scale. The illuminated retinal area is much too large, while the virtual image is too small and much too close to the eye.

Fig. 3B.—This graphic optical construction depicts the dioptric principles involved in Figure 3A. The principal planes of the eye, the anterior principal focus (F_1), the posterior principal focus (F_2), the optic axis of the eye, the principal points (P_1 and P_2), the illuminated retinal area (I_1RI_2), the far point of the eye (F) and the virtual image (V_1FV_2) all are indicated. The lines used for the construction of the enlarged erect virtual image also are shown.

The geometrical relationships depicted permit the computation of the size of the virtual image in the plane of the far point. From the similar triangles $F_1K_1L_1$ and $F_1V_1V_2$ it is apparent that $\frac{F_1P_1}{K_1L_1}=\frac{F_1F}{V_1V_2}$. Since F_1P_1 is the anterior focal length and is equal to 17.05 mm. and since $K_1L_1=I_1I_2$, $V_1V_2=\frac{I_1I_2(17.05+P_2F)}{17.05}$ P_2F is the distance of the far point from the second principal point and is known from the amount of hypermetropia that is assumed.



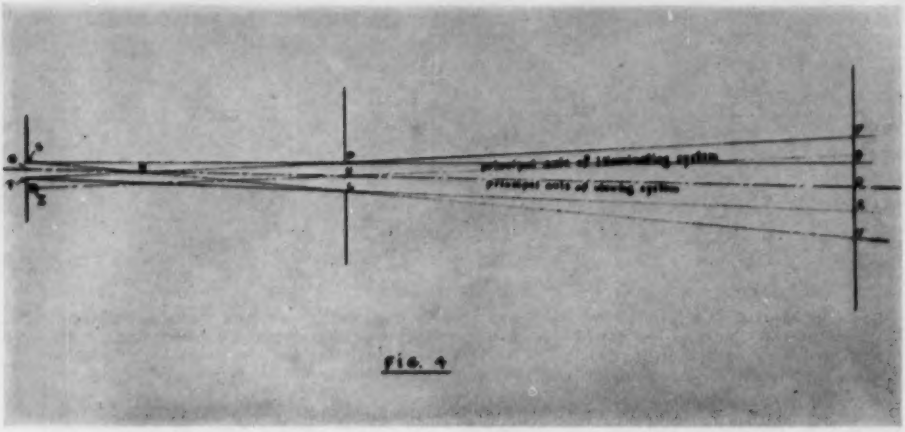


Fig. 4.—This geometric drawing shows, in cross section, the field of vision available to the observer behind the sight hole of the ophthalmoscope and also the slight divergence that exists between the viewing system and the illuminating system. The drawing is not to scale, because the pupillary and ophthalmoscopic apertures are so very tiny relative to the distance between the ophthalmoscope and the subject's eye and also to the distance between the plane of the pupil and the far point of the hypermetropic eye.

The image of the filament in the mirror or in the face of the prism of the ophthalmoscope is projected forward into a hypermetropic eye. It is interrupted by the retina before it can come to a focus because the eye is too short. However, the illuminated retinal area acts as a primary source of light and is conjugate with its virtual image in the plane of the far point. The return light from the eye appears to come from this virtual image in the plane of the far point.

SGT represents the aperture in the ophthalmoscope. It has been assumed to be 2.5 mm. long. *PUL* is the diameter of the subject's pupil, here assumed to be 4.0 mm. *FBORV* represents a part of the far-point plane of a hypermetropic eye. The distance between Points *G* and *U* is 300 mm. By simple geometry the distance *GN* can be found to be 115.4 mm.; and the distance *NU*, 184.6 mm. The Lines *SV* and *TF* indicate, in cross section, the limits of the field of view into the observed eye. As explained in the text, only points from the area represented in cross section by the distance *BOR* can send equal cones of light back through the pupil and into the sight hole *SGT*. Points located beyond this central area can send only progressively smaller angles of light through *SGT*, because the iris obstructs some of the rays. Because of this rapid decrease in brightness, the actual limits of the observer's field of view actually lie about half-way between *F* and *B*, and *R* and *V*.

Below the sight hole is the image of the filament, in cross section, in the face of the prism. Its edge is separated from the edge of the sight hole by a vertical distance of 1.0 mm.

the retina in the plane of the far point (Figs. 3A and 3B). Since the size and location of the illuminated retinal area and also the location of the far point have already been determined for each of the five selected amounts of hypermetropia, it is easy, by applying the proportions between the similar triangles of a graphic construction, such as Figure 3B, to ascertain the diameters of the virtual images of the illuminated retinal areas. For 0.5, 1.0, 2.0, 3.0, and 4.0 D. of hypermetropia the virtual images will be 53.4×41.5, 29.3×23.3, 17.0×14.0, 12.8×10.7, and 10.8×9.3 mm. in cross section, the first number being the horizontal axis and the second number being the vertical axis of the elliptic area.

The Field of View Through the Ophthalmoscope in Hypermetropia.—The size and position of the virtual images of the illuminated retinal areas for selected amounts of hypermetropia have been determined. It now becomes necessary to compute the size and position of the field of vision available to the observer while he is looking through two small openings separated by a certain distance. Reference to Figure 4 will show how the observer's field of view is limited: first, by the diameter of the ophthalmoscopic sight hole; second, by the diameter of the

pupil of the subject's eye, and, third, by the distance between the two openings. Point *S*, the upper limit of the ophthalmoscopic aperture, can transmit light rays emanating only within the angle delineated by Points *B* and *V*. Point *T*, the lower limit of the aperture, can transmit only rays arising between Points *F* and *R*. Likewise, every other point between *S* and *T* is limited by the angle of its projection through *P* and *L*, the extremes of the pupillary opening. Thus, while the whole field of view extends from *F* to *V*, no single point between *S* and *T* can transmit rays emanating from this whole field. Only rays from a much smaller area, represented in cross section by *BR*, will pass through every point in the aperture *ST*. Light rays emanating from the area peripheral to this central elliptical area —from the area represented in cross section by the distances *FB* and *RV*—will pass through only a part of the aperture. Consequently, that part of the virtual image which is covered by the central part *BR* of the observer's visual field will appear brighter than the part peripheral to it. The latter will become increasingly less bright with increasing distance from the central area. Reference to Figure 4 shows that from *B* toward *F*, and from *R* toward *V*, each successive point subtends an increasingly smaller angle past Point *P*, or Point *L*, and through as large a part of the opening *ST* as is possible.

In computing the size of the field of vision available to the observer it seems reasonable to limit its radius to the distance from its center *O* to half-way between *F* and *B* (or *R* and V). From *B* to *F* and from *R* to *V* there is a uniform decrease in brightness to almost zero. In fact it would be zero if it were not for scattered internally reflected light within the eye. Half-way between these points is a good practical boundary for the observer's eye to notice a marked decrease of illumination. Also, an observer seldom presses his eye tightly against the ophthalmoscopic sight hole, and this slight separation between the eye and sight hole causes a slight constriction in the available field of view.

Since the following distances are known: the size of the ophthalmoscopic aperture (assumed to be 2.5 mm.); the diameter of the subject's pupil (assumed to be 4.0 mm.); the distance between the ophthalmoscope and the subject's pupil (approximately 300 mm.), and the distances of the planes of the far points from the posterior principal planes of the eye, it becomes possible by applying the geometry of similar triangles to a construction such as Figure 4 to compute the cross sectional sizes of *RB* and *BF* (or *RV*) for various amounts of hypermetropia. For the 0.5, 1.0, 2.0, 3.0, and 4.0 D. used in this article, *BF* is equal to 16.7, 8.4, 4.2, 2.8, and 2.1 mm., respectively, and *RB* is equal to 13.9, 8.9, 6.4, 5.6, and 5.2 mm., respectively. From this it follows that the diameters of the field of view, extending from half-way between *F* and *B* to half-way between *R* and *V*, are 30.6, 17.3, 10.6, 8.4, and 7.3 mm., respectively.

Overlapping of the Field of View and the Image Area in Hypermetropia.—If the observer's field of view is not concentric with the image of the illuminated retinal area, which is the case for all electric ophthalmoscopes with a sight hole located immediately above the edge of the mirror or prism, there will be an overlapping of the two areas. Unless the image-area is much larger than the field-area, part of the latter will not be covered by the former and therefore will appear unilluminated except for some internally scattered light.§

As already described, in the usual modern electric ophthalmoscope the aperture is located above the light source (the image of the filament). Therefore, the field of view and the virtual image of the illuminated retinal area are not concentric. Furthermore,

§ In the original reflecting (nonelectric) ophthalmoscopes a circular aperture penetrated the center of the concave reflecting mirror, thereby making the viewing and illuminating systems concentric. This resulted in a uniformly illuminated fundus reflex in which opacities of the media, especially the lens, were sharply outlined.

their sizes are not identical; nor are their outlines, the field of view being circular and the image area being elliptical. It therefore becomes necessary to know the distances of the centers of these two areas from each other. In Figure 4, Point *I* represents the center of a vertical cross section of the filament image in the edge of the mirror or prism. The filament image has been assumed to be 1.2 mm. in diameter. Its upper edge may be assumed to be separated vertically from the lower edge *T* of the sight hole by a distance of 1.0 mm. The diameter of the sight hole has been taken to be 2.5 mm. Thus, Points *G* and *I* are separated vertically by a distance of 2.85 mm. (one-half of 1.2, plus 1.0, plus one-half of 2.5). This provides the information that, at a distance of 300 mm. from their point of intersection, at *U*, in the center of the subject's pupil, the principal axis of the viewing system and the principal axis of the illuminating system are separated by a distance of 2.85 mm. Knowing the inclinations of the two principal axes, it is easy by applying either simple trigonometry or simple geometry to this information to compute the separation of the two axes at the various distances where the virtual images are located. Thus, for the chosen 0.5, 1.0, 2.0, 3.0, and 4.0 D. of hypermetropia the center of the visual field is 19.0, 9.5, 4.8, 3.2, and 2.4 mm., respectively, below the center of the virtual image of the illuminated retinal area. It is apparent that the separation between the center of the visual field and the center of the virtual image decreases with the amount of hypermetropia.

For each of the five amounts of hypermetropia selected for mathematical analysis under the conditions specified, the following data have been obtained: the vertical diameter of the virtual image in the plane of the far point, the diameter of the field of view in the plane of each far point, and the vertical separation of the centers of the virtual image and the field of view. It now remains to determine the linear extent of the overlapping of these two areas in the

TABLE 1.—*Theoretical Calculations in Hypermetropia*

Hypermetropia, D.	Vertical Radius (½ Length) of Virtual Image, Mm.	Radius of Field of View, Mm.	Separation of Centers in Vertical Meridian, Mm.	Amount of Overlapping in Midvertical Meridian, Mm.	Ratio of Vertical Extent of Bright Area to Dark Area	Appearance of Pupillary Area (Dark Area Marked by Diagonal Lines)
0.5	20.8	15.3	19.0	17.1	1.3:1.0	56% Light
1.0	11.7	8.7	9.5	10.9	1.7:1.0	63% Light
2.0	7.0	5.3	4.8	7.5	2.4:1.0	71% Light
3.0	5.4	4.2	3.2	6.4	3.2:1.0	6% Light
4.0	4.7	3.7	2.4	5.9	4.2:1.0	81% Light

vertical meridian. This is very easily obtained from the fact that the vertical overlapping equals the sum of the vertical radius of the virtual image and the radius of the field of vision minus the separation of their centers (Table 1). The observer will see the area of overlapping as a higher bright area separated by an elliptic boundary from a lower relatively dark area, because, as already mentioned, the center of the virtual image of the illuminated retinal area is above the center of the field of view. The ratio of the height of the bright area to the height of the relatively dark area is easily obtained after subtracting the vertical amount of overlapping from the diameter of the field of view. All the foregoing data are shown in Table 1; also, the proportion (vertically) of the illuminated to the dark area is given. The observer automatically refers emitted light from the eye (and also lack of emitted light) to the pupillary area.

Myopia

In the development of the explanation of the variation in the fundus reflex with the degree of hypermetropia every step has been exemplified by computations. In a sense this is absurd, as the conclusions drawn from these computations can apply only to an ophthalmoscope, an observer, and an observed eye meeting the exact specifications mentioned as to size of filament image, size of aperture, distance of aperture above filament image, distance from observed eye, and size of observed pupil. Also, no accommodation was assumed for the observed eye. No two ophthalmoscopes ever are exactly alike. Then, also, the filament image must be perfectly horizontal when the ophthalmoscope is in the vertical position. Many ophthalmoscopes are out of adjustment and show tilted filament images. Furthermore, the optical elements of an eye vary considerably from person to person and do not necessarily conform to those of the standard eye. Errors of refraction need by no means all be on an axial basis. For these reasons, in the discussion of myopia the changes in the fundus reflex will be described more qualitatively. Results of computations will be mentioned chiefly in order to orient the reader as to the magnitude of the images and distances involved.

The Light from the Ophthalmoscope.—In the section on hypermetropia it was shown that the 3.0×1.2 mm. source of light in the face of the prism 300 mm. away will come to a focus in a standard nonaccommodating eye of 58.6 D. of refracting power at a distance of 25.7 mm. behind the corneal vertex. This image will be located on the retina of an unaccommodated eye only if that eye is myopic to the extent of 3.3 D., which is the same as having its far point at 300 mm. in front of the corneal vertex. In lesser degrees of myopia the retina will intercept the entering light rays before they can reach a focus, and in greater degrees of myopia the retina will intercept the rays as they are diverging from a focus in front of the retina. The illuminated retinal area will be larger than the image by an amount that will depend partly on the size of the exit pupil and partly on the position of the retina.

The Location and Size of the Illuminated Retinal Area.—In myopia the far point lies in front of the eye. If the myopia is axial, the location of the retina in various amounts of myopia can be computed from the general formula for object and image distances. Thus, for 0.5, 1.0, 2.0, 3.0, 4.0, and 5.0 D. of myopia the retina is located at 23.0, 23.2, 23.6, 24.0, 24.5, and 24.9 mm., respectively, from the second principal point.

By the same simple geometric method used for hypermetropia it is possible to compute the size of the illuminated retinal area for each of these selected amounts of myopia. Since in this presentation only the vertical diameters of the elliptical illuminated retinal areas are of interest, only these have been obtained. They are, respectively, 0.28, 0.24, 0.17, 0.09, 0.15, and 0.23 mm.

With the foregoing data at hand, it is possible, by using the general formula relating object and image sizes to object and

image distances, to obtain the size of the image of the illuminated retinal area as formed outside (in front) of the eye by the dioptric apparatus of the myopic eye. For the chosen 0.5, 1.0, 2.0, 3.0, 4.0, and 5.0 D. of myopia, the vertical extent of the image at the far point is 31.6, 13.4, 4.7, 1.6, 1.9, and 2.4 mm., respectively. These images are centered on the principal axis of illumination—the line connecting the center of the filament image in the face of the prism with the center of the subject's pupil.

The Changes in the Fundus Reflex.—The cause of the change in the appearance of the fundus reflex with the amount of myopia lies primarily in the fact that the aperture of the ophthalmoscope is located above the principal axis of illumination. This can be understood more readily by reference to a graphic construction such as Figure 5.

In myopia of less than 3.3 D. the image of the illuminated retinal area will tend to form beyond the ophthalmoscope—at a greater distance than the 300 mm. from the observed pupil. In myopia of more than 3.3 D. the image of the illuminated retinal area will be formed in front of the ophthalmoscope—at a smaller distance than 300 mm.

Myopia of amounts greater than 3.3 D. will be considered first. The vertical size of the image at the several far points has been determined. These images are centered on the principal axis of illumination. For the chosen 0.5, 1.0, 2.0, and 3.0 D. of myopia, the top of each corresponding image will be 15.8, 6.7, 2.4, and 0.8 mm., respectively, above the axis. The first three of these images extend higher than the lower margin of the aperture, which is 1.6 mm. above the axis. Therefore, light rays tending to converge toward the upper extremities of these images are able to pass through the aperture and become visible to the observer as light emerging from the upper part of the observed pupil. Light rays emerging through the lower part of the observed pupil are blocked by the structure of the ophthalmoscope below the sight hole and therefore are not seen. This causes the pupillary area from which they emerge to appear dim. In fact, this area would appear

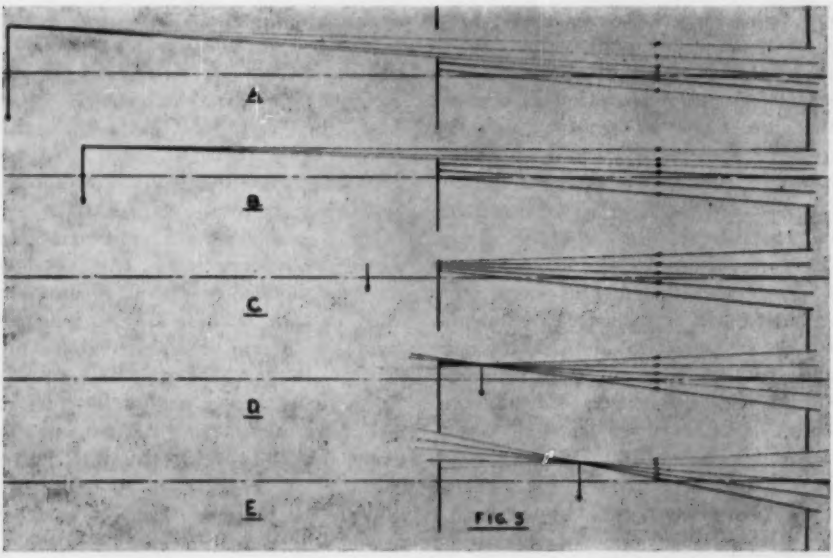


Figure 5 (Legend on opposite page)

Fig. 5.—A schematic graphic construction, of a vertical midline cross section, which shows the emergence of rays through the pupils of eyes with different amounts of myopia as seen by an observer behind the aperture of an ophthalmoscope. The light rays are converging toward real inverted images of the illuminated retinal areas. These images if permitted to be formed would be located in front of the eyes at the respective focal points. Only rays directed toward the upper extremities of the images are shown. Those which are directed toward points lower down are not shown, as, for the most part, hardly any of them even approach the aperture of the ophthalmoscope and therefore they are invisible to the eye of an observer.

The drawings are not to scale. The horizontal distances involved are so very much greater than the vertical distances that it is impossible to make a scale drawing.

A, B, C, D, and *E,* respectively, represent, in a very approximate way, the pupillary phenomena as seen in 0.5, 1.0, 3.0, 4.0, and 6.0 D. of myopia.

In the three upper drawings, which deal with myopia up to 3.3 D., it is apparent that not all of the rays can pass through the aperture of the ophthalmoscope, which is too high for many of them. The rays which do not pass obviously cannot be seen by the observer, and that part of the pupillary area from which they emerge will seem relatively dim. Up to 2.5 D., as the myopia increases, progressively fewer of the upper rays emerging from the pupil are able to pass through the sight hole. This decrease proceeds from below upward in the pupillary area so that finally only rays emerging from the upper pupillary margin are able to pass through the sight hole. In myopia of 2.5 to 3.3 D. no rays at all can pass through the aperture (*C*), as the images fail to reach the height of the lower margin of the aperture and also are located too near the aperture.

The lowest ray, on its way to the upper end of the image, that is able to clear the bottom of the aperture, designates, at its point of emergence in the pupillary area, the lowermost point of the curved boundary (concavity upward) that separates the upper bright area of the pupil from the lower dim area. All rays that proceed to other points in the image lower down than the upper extremity must emerge from the pupillary area at higher levels than the limiting ray. Thus, for that part of an image which tends to be reached by rays able to pass through the aperture, a progressively decreasing number of rays, emerging from above down through the pupil, can pass toward it. As a consequence, the bright areas are brightest at their upper margins, and from there downward there is a gradual decrease in brightness until no rays that are directed toward the image can pass. There always are extraneous, internally reflected rays, not directed toward the image, that emerge from the dim area and pass through the sight hole of the ophthalmoscope. Therefore, the dim area never is without any light. An observer will select, as the boundary between the bright and dim area, a level that is higher than the actual curved boundary from below which no directed rays can pass through the ophthalmoscopic aperture. This level will vary with the keenness of each observer's light sense.

The two lower drawings illustrate the optical conditions, in the vertical midline, in myopias of greater amount than 3.3 D. Here real images are formed between the ophthalmoscope and the observed eye. As the myopia increases an increasing number of rays that emerge through the lower pupillary area are able to pass through the aperture after divergence from the upper part of the image. Thus, as the myopia increases an increasingly larger part of the pupillary area, from below upward, becomes bright. Here, also, limiting rays can be drawn from the lowest point of the aperture, through the upper extremity of the image, to the pupillary area. Any ray directed to a point on the image below the upper extremity, if it is to pass through the aperture, must emerge through the pupil at a lower level than the limiting ray. This limitation on the visibility of emerging rays once more produces a gradual transition in brightness, the lowest part of the pupil being the brightest. Each observer again will make his own estimate of the level of the boundary between the bright and dim areas, and it will be lower than the actual theoretical boundary established by the limiting rays.

It will become apparent from a study of Drawings *A* and *B* that in myopias of less than 2.5 D. the observer can allow more and more of the blocked lower rays to pass through the sight hole by withdrawing or moving backward from the observed eye. This will extend the width and increase the intensity of the bright area from above downward. The opposite effect can be produced by advancing with the ophthalmoscope. A study of Drawings *D* and *E* will show that in myopias of more than 3.3 D. a similar increase in width of the bright area, from below upward, and a simultaneous increase in intensity will occur upon moving backward with the ophthalmoscope. The opposite effect will occur upon moving forward.

dark if it were not for the emergence of scattered internally reflected light.

The image that tends to be formed in front of an eye with 3.0 D. of myopia would extend only 0.8 mm. above the principal axis, and none of the rays emerging from the observed eye can clear the lower edge of the aperture, which, at 1.6 mm. above the axis, is too high for them (Fig. 5C). Therefore, the whole pupil will appear uniformly dim.

For every myopic image which is located beyond the ophthalmoscope and which also is higher than the lowest part of the aperture there is a limiting ray of visibility which emerges from the pupil. This is the ray which barely clears the lower edge of the aperture, in the midline, on its way to the upper extremity of the image. Any ray which emerges from the pupil below this limiting ray will not be able to pass through the aperture and therefore will not be visible. Furthermore, all rays directed through the pupil to points lower down on the image than the upper extremity must emerge from the pupillary area at higher levels than the limiting ray. Otherwise they will not clear the aperture and thus will not be seen. These limiting rays can be determined easily by applying simple geometry to a graphic construction such as Figure 5. For 0.5, 1.0, and 2.0 D. of myopia the limiting ray emerges in the pupillary midline at 0.9 mm. below the midpoint, 0.6 mm. below the midpoint, and 0.4 mm. above the midpoint, respectively. This, in turn, means that for an apparent pupillary diameter 4.5 mm. there will be bright illumination of the upper 70%, 60%, and 40% of the pupillary midline for the corresponding 0.5, 1.0, and 2.0 diopters of myopia.

Below the upper extremity of the image, each point that would be able to receive rays through the aperture also has its limiting ray. Any ray emerging through the pupillary area below such a ray cannot clear the lower edge of the sight hole. The limiting ray for each point in the image midline, from above down, arises at successively higher points in the midpupillary line. This means that the illuminated upper part of the pupillary area appears brightest at its upper extremity and that this brightness gradually decreases from above down until the boundary established by the limiting rays to the upper extremity of the image is reached. Actually, no observer will be able to see the theoretical boundary between the bright and the dim portions of the pupillary area, because the two areas blend so gradually and also because of the extraneous internally reflected light that emerges through the dim part of the pupillary area. Each observer, according to his judgment, will estimate this curved boundary to be somewhat above the true boundary. Thus, the computed percentages of height of illuminated area in the midline are highly theoretical, and they are considerably greater than those estimated in practice.

Astigmatism

The pupillary light phenomena which have been described result from the linear displacement of the viewing system of the ophthalmoscope relative to the illuminating system. In the usual position of the ophthalmoscope this refers to the vertical meridian. For other meridians the observer must hold the ophthalmoscope lengthwise in the desired meridian.

Since astigmatism involves a meridional distribution of a refractive condition, only the resultant in the observed meridian has an effect on the appearance of the fundus reflex. This part of the astigmatic error combines algebraically, as it were, with any spherical error that is present to determine the appearance of the illumination in the pupillary area.

By turning the ophthalmoscope into several meridional positions an observer often can detect, by differences in the appearances of the fundus reflex, astigmatic errors as low as 0.75 D.

Observations

Reasons have been given why the actual appearance of the illumination in the fundus

reflex differs from theoretical deductions. An important additional reason is accommodation by the observed person. Even though instructed to gaze off into the distance, the average person will accommodate automatically as soon as an observer moves into his line of vision with an instrument. Consequently, all eyes will appear to be either more myopic or less hypermetropic than they really are. Even an elderly person of 60 can accommodate up to 0.5 D. easily and readily. Thus, only the range in which a refractive error lies can be approximated. Obviously, this fundus-reflex method of estimating refraction does not compare with retinoscopy in accuracy. On the other hand, it is almost instantaneous, and even when done in several meridians in order to detect the existence of appreciable astigmatism it takes almost no time to perform.

In observing a pupil note must be made of the level where the boundary between the bright and dim area crosses the vertical midline of the pupil. Then, the ophthalmoscope should be rotated into one or two oblique positions and also into the horizontal. Similar observations should be made in the several meridians with respect to the pupillary midlines in those meridians.

Each observer must establish his own correlations for the particular instrument and working distance that he may use. My own observations are given briefly in Tables 2 and 3. They are valid only for my particular ophthalmoscope and can be transferred only approximately to another instrument. The observations were made on eyes in which no cycloplegic was used. The patients were told to try to maintain fixation for distance during the very brief period of observation.

TABLE 2.—*Observations in Hypermetropia*

Hypermetropia in the Observed Meridian, D	Approximate Part of Pupillary Diameter That is Brightly Illuminated (Oriented for the Vertical Meridian)
0 to 1.0	Upper ⅕ to < upper ⅓
1.0 to 2.0	Upper ⅓ to < upper 3/5
2.0 to 3.0	Upper 3/5 to < upper ⅘
3.0 to 4.0	Upper ⅘ to < upper ¾
< 4.0	Gradually from upper ¾ to whole pupillary area; however, the over-all brightness decreases with the increased divergence of the emerging rays.

TABLE 3.—*Observations in Myopia* *

Myopia in the Observed Meridian, D.	Approximate Portion of Pupillary Diameter That is Brightly Illuminated (Oriented for the Vertical Meridian)
0 to 1.0	Upper 2/5 to upper ⅘
1.0 to 2.5	Upper ¼ to almost nothing
2.5 to 3.5	The whole pupillary area is dark
3.5 to 4.5	Narrowest possible lower crescent to lower ¼
4.5 to 5.5	Lower ¼ to lower ⅓
5.5 to 6.5	Lower ⅓ to lower ½
> 65.	Gradually, from lower ½ to whole pupillary area; the over-all brightness decreases because of the increased divergence of rays from the images in front of the eyes.

* In myopia, if the observer will back away slightly, with his ophthalmoscope, to a greater distance than 12 in., he will see the bright band increase slightly in width. Reference to Figure 5 will help explain this.

Summary

A method is described which enables an observer to estimate instantaneously the approximate refraction of an observed eye in the meridian that corresponds to the position (length) of the ophthalmoscope. By turning the ophthalmoscope into one or more additional positions, such as horizontal and oblique, the observer can determine whether or not a substantial amount of astigmatism is present. This method is in no sense a substitute for retinoscopy, but it can be useful as a means of obtaining a quick approximation of the refractive state of an eye.

While looking at an eye with a modern electric hand ophthalmoscope from a distance of about 12 in. one seldom sees a uniformly bright fundus reflex in the pupillary area. Usually the pupillary area is divided into two zones by a somewhat indefinite curved boundary. One portion is relatively brightly illuminated, and the other portion appears dim or even dark. The extent of these two zones relative to each other, in the midline of the pupil corresponding to the position of the ophthalmoscope (usually vertical at the beginning of an examination), depends upon and varies with the refraction of an eye in the meridian that corresponds with the length of the ophthalmoscope. Thus, the division of the fundus reflex into two parts, a bright area

and a dim area, can be used clinically for approximately estimating the refraction of an eye.

The described phenomenon is made possible by the construction of the ophthalmoscope—specifically, by the upward displacement of the sight hole relative to the axis of illumination. In a hypermetropic eye not all of the rays that emerge through an observed pupil, as though coming from an upwardly displaced enlarged virtual image behind the retina at the far point, can pass through the aperture of the ophthalmoscope, which is too high for some of them. In a myopic eye not all of the rays emerging from the retina, on their way to a conjugate image in front of the eye lower down than the aperture, can pass through the latter. That portion of the pupillary area from which the emerging rays cannot reach the aperture will appear dimly illuminated to the observer. Since the conjugate images of illuminated retinal areas vary in position and size with the refractive state of an eye, the fundus reflex will vary accordingly.

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Subconjunctival Suture in Cataract Operation

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Since 1950 I have been using a new type of subconjunctival suture for closing the incision in the cataract operation. The technique of this type of suture is described in this article, and the results obtained with its use are reported and compared with those obtained in an equal number of operations performed in other cases, with the same number of stitches, the same material, and so forth, but with the stitches placed in the usual manner.

This suture had its origin in my desire to obtain a firm closure of the wound which would not expose the anterior chamber to fistulization and which would not have the inconveniences associated with multiple stitches and the difficulties encountered in removing them.

The perfect tolerance of the eye for pure silk, when the material is used in cataract operations which are performed with the conventional sutures as well as in keratoplasties, suggested to me the idea of leaving the sutures subconjunctivaly, in order to prevent the inconveniences caused by the friction of the knots, namely, the troublesome removal of the stitches and the possibility of filtration of the aqueous humor through the wound.

Several techniques were tried (Fig. 1), and two among them were selected as being the most adequate. At first, only one stitch of this kind was placed in flaps which were cut with a Graefe knife, until I was convinced, by observation of the postoperative course, that the material was perfectly tolerated. Three subconjunctival and two complementary stitches of the conventional type were then placed, and those of the conventional type were removed on the ninth day.

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The technique outlined in Figure 2, which was finally adopted because of its great simplicity, was used along the entire wound, which made necessary the preliminary cutting of a conjunctival flap of 180 degrees for coverage of the entire incision.

This technique was used in the 50 cases upon which this study is based. It is as follows:

1. Incision of the conjunctiva with scissors, in the upper half, 5 mm. from the limbus.

2. Dissection of the conjunctival flap, without involving the subconjunctival tissue, up to beyond the sclerocorneal limbus.

3. Hemostasis, if it is necessary, with a glass rod heated in a flame. If the flap is cut strictly from the conjunctiva, hemorrhage is minimal. Dissection is easier if 1 cc. of air is subconjunctivally injected before one starts to section the conjunctiva.[1]

4. The globe is firmly fixed by the tendon of the rectus medialis muscle (in the right eye) or of the rectus lateralis muscle (in the left eye), and a paracentesis of 30 degrees is made with the keratome, at 9:30 o'clock, exactly at the level of the apparent sclerocorneal limbus, in such a way that a small part of the cornea is left free between the section and the insertion of the conjunctiva.

5. The conjunctival flap is fixed with a fine untoothed dissecting forceps, and the section is enlarged to the left with scissors, parallel with the plane of the iris, in order to obtain a good bevel, to traumatize the iris as little as possible, and to leave a subconjunctival lingulate flap of cornea along the entire incision. The lingulate flap is necessary for insertion of the sutures, and care should be taken not to take much of the sclera. In this way an incision of 180 degrees is obtained, with a subconjunctival corneal lingulate flap throughout its extent

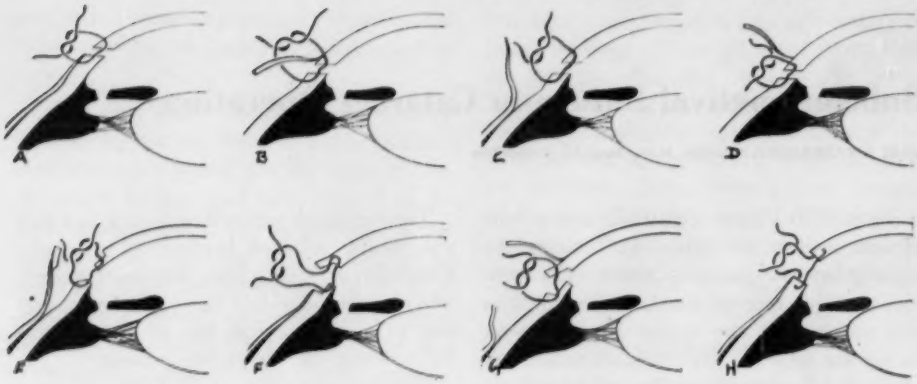


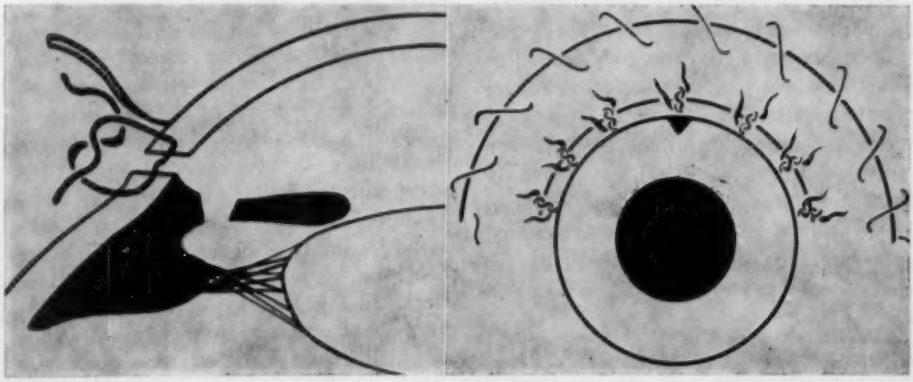
Fig. 1.—Various types of corneoscleral types of suture investigated. *A* and *B*, conventional sutures; *C*, *D*, and *G*, subconjunctival sutures; *E*, *F*, and *H*, intracorneal sutures.

and with an endothelial section far enough from the anterior chamber and the base of the iris to prevent the formation of anterior synechiae.

6. Sutures are placed with the following technique: The corneal lip of the wound is fixed with the suture forceps at the anterior edge of the cut surface, a little to the left of the place where the suture is to be placed, but as close to it as possible, so that one arm of the forceps is on the anterior surface of the cornea and the other arm is on the cut surface. In no case should the forceps grasp the entire thickness of the cornea.

The needle, placed exactly at the tip of the needle-holder, at right angles to it and held by its posterior third, a little below the eye, is inserted in the anterior surface of the corneal flap 0.5 mm. from the cut edge so that its point emerges in the center of the cut surface. When the point of the needle projects from 0.5 to 1 mm., its further advance is stopped and the suturing forceps is transferred from the corneal to the scleral lip of the wound, to fix the anterior surface of the scleral section, which it grasps by the external aspect at the center of the cut surface. The needle, which was inserted into the cornea and has already emerged through the corneal cut surface, then enters the center of the cut surface of the scleral lip to emerge from the external surface of the sclera 0.5 or 1 mm. behind the cut edge. During all these stages the needle-holder

Fig. 2.—Multiple subconjunctival suture. The conjunctival flap is sutured with a 00000 gut suture.



should push the needle with a movement of rotation equal to that of the curve of the needle, until the latter strikes the cornea; in this way, the point of the needle will project as far as possible and the needle can be grasped at the juncture between its middle and anterior thirds so as not to injure the sharpness of its point.

If for some reason the corneal lingulate flap is very narrow, the suture passes through the conjunctiva. In the cases in this study this occurred in less than 3%. It seems to have had no serious consequences, since a secondary healing of the conjunctiva above the stitch was observed in the postoperative course.

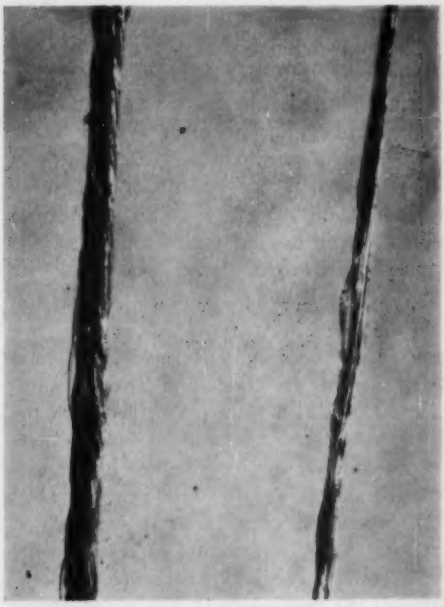


Fig. 3.—Comparative microphotograph of Kalt's (braided) and my (nonbraided) silk sutures.

The original material used by me in suturing was the same in all cases, namely:

1. Pure (raw) silk composed of seven cocoon threads 0.04 mm., nonbraided and tinted with a 6:1000 methylene blue solution in order to facilitate management and to permit loss of color, because silk so tinted becomes invisible within a few hours after having being placed (Fig. 3).

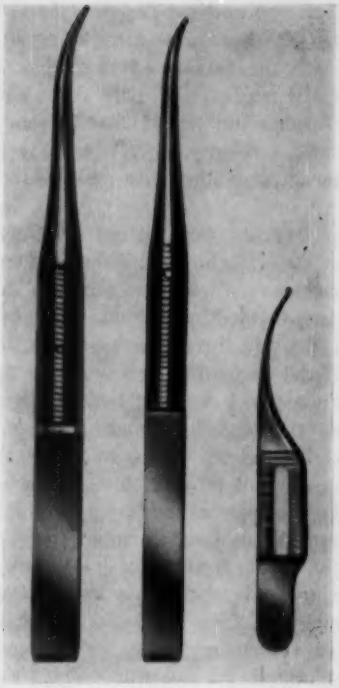


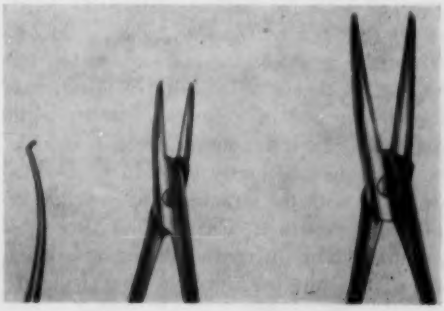
Fig. 4.—My hemostatic pincers, needle-holder, and forceps for iridectomy and suture.

2. A suture needle 4 mm. long, with the sharp edge in the convexity (Grieshaber No. 83).

3. A special very delicate needle-holder with a slightly curved point, with or without a lock between its jaws (Figs. 4 and 5) for No. 83 needles.

4. A very fine elbow-shaped forceps with one tooth in one jaw and two in the other (Figs. 4 and 5).

Fig. 5.—Jaws of instruments in the Figure 4.



5. The conjunctival flap was fixed with plain 00000 absorbable surgical (gut) sutures with the Davis and Geck No. 1611 Atraumatic needle.

6. Adson's untoothed forceps and my hemostatic forceps (Figs. 4 and 5) were used as needle-holders for the conjunctival suture.

Seven stitches were placed in all cases: one previous stitch at 12 o'clock and three complementary stitches on each side. Every stitch was formed by a simple loop situated in the anterior three-fourths of the thickness of the tissue and was tied with a surgical knot, which was not tied too tight, to prevent traction that might deform the cornea, leading to fold formation. When a stitch was not properly placed or when it caused deformation on being tied, it was systematically replaced by another.

In the cases observed in this group, the subconjunctival stitches remained in place indefinitely in 25% of the cases; in most cases, however, the stitches were spontaneously eliminated between 20 and 30 days after the operation. Only when a stitch perforates the conjunctiva and produces a sensation of a foreign body is it necessary to remove it. This is done as if the stitches were of the conventional type, but in all cases this maneuver is far simpler because of the lack of irritation of the eye and the firmness of the wound, inasmuch as the removal is made 15 days after the operation. To remove these stitches, it is not necessary for the patient to lie down, because it is advantageous to perform the maneuver either with the patient seated in the operating chair with the aid of the surgical microscope or with the patient resting his head on the chin-rest of the slit lamp.

In order to assess the results obtained by the use of this type of suture, operations were performed in a series of cases with use of the new technique in alternation with the technique previously used, in which the flap is cut with the Graefe knife as follows:

Radiate puncture. Counter puncture apparent at 1 mm. in front of the limbus. Section of the internal third, as the blade of the knife continues to be introduced up to near its base. Section of the external third with withdrawal of this and of either the central or the middle third with two ample sawing movements, directing the cutting edge backward during the first movement in order to cut a small scleral tongue and forward during the second movement to put a limit to the scleral tongue and to the conjunctival flap.

The number of sutures placed was seven in all cases, and for the placing of the sutures in both techniques the same material and instruments were used.

The conventional sutures were removed between the 10th and the 12th days, using for this purpose Shaaf's forceps for fastened stitches and a piece of a razor blade mounted in a needle-holder. Removal was carried out with the eye under anesthesia by instillation of a 5% cocaine collyrium with epinephrine and under control of the surgical microscope.

In order to make an equitable comparison between these two types of sutures, we selected 100 consecutive operations of total extraction of the crystalline lens for cataract, 50 of which were performed with the suture commonly used and 50 with the new subconjunctival suture. The cases were distributed as follows: (1) senile cataract, 89; (2) myopic cataract, 4; (3) complicated cataract, 5; (4) congenital cataract, 2. Of these patients, 33 had simultaneous operations in the two eyes; 34 had an operation only on one eye; 13 of the patients were monocular, 12 of them having lost one eye as a result of various complications following cataract surgery. All the operations had the following factors in common:

1. Premedication.
2. Anesthesia.
3. Akinesia.
4. Incision of 180 degrees in the upper half of the limbus.
5. A previous suture.
6. Peripheral iridectomy at 12 o'clock.
7. Total extraction.
8. No loss of vitreous humor.

9. Miosis by irrigation of the anterior chamber with acetylcholine solution.

10. Six complementary stitches (Fig. 2).

11. Simultaneous operation on both eyes, or else the eye on which an operation was not performed was uncovered on the day on which the operation was performed.

12. Authorization to the patients to move freely in bed from the first moment after the operation and to get up by themselves to make their personal toilet as soon as the effect of premedication had worn off.

13. First dressing on the second or third day.

14. Discharge of the patients from the clinic the third day and return of the patients to their homes, with subsequent visits to the office for further care and treatment on an ambulatory basis.

15. No bandage, provided that there was not too much photophobia and lacrimation to make this tolerable.

16. The day the bandage was removed, the patient was provided with temporary glasses with spheric correction, without measurement of the visual acuity.

17. Cases in which there were accidents such as rupture of the capsule or of the hyaloid membrane were excluded, because it was considered that such accidents might process, the occurrence of postoperative astigmatism, and so forth and would, therefore, differ from and be unrelated to the question of suture which was under investigation in these observations.

In my opinion, the difference in the results between the incision performed with a Graefe knife and the incision performed with a keratome and scissors (Daviel) involves the iris (atrophy), and this has been dealt with in a previous report.[2]

Howard Reed[3] recently reported the results of a comparative study of 180 cases in which the incision was made either with a Graefe knife or with a keratome and scissors (Daviel). He concluded that there was no difference in the results of the two methods and that the choice of either method therefore depends merely upon individual preferences.

Consequently, I believe that the differences that may be observed in the results of these two series of cases (which are the basis of this study) are attributable to the different types of suture used in the two groups, since all the other surgical stages were comparable to each other in the two series.

With the technique of subconjunctival suture, the operation takes longer and loses in cleanness and spectacular qualities and in the postoperative stage the patients for more than three weeks have red eyes as a result of conjunctival hyperemia. On the other hand, the operation is much safer, the postoperative accidents are fewer, the patients can move freely from the very first moment after the operation, and they experience neither the unpleasant sensation caused by the stitches nor the fear of their removal; the period of bandaging is greatly diminished and recuperation of visual acuity is rapider. Postoperative astigmatism also occurs less frequently. A glance at the accompanying Tables is sufficiently eloquent for appreciation of the superiority of subconjunctival sutures over the sutures commonly used.

In regard to postoperative accidents, I found delay in the reformation of the anterior chamber in 24%, detachment of the choroid in 4%, and hyphema in 2% during removal of the stitches with the conventional suture, in comparison with delay in the reformation of the anterior chamber in only 2% with the use of the subconjunctival suture.

In the Table 2 a diminution of more than six days in the period of bandaging can be

TABLE 1.—*Postoperative Complications*

Complication	Commonly Used Suture		Subconjunctival Suture	
	Cases	%	Cases	%
Flat chamber after the first or second dressing	7	14	1	2
Detachment of the chorold	2	4	0	
Loss of the anterior chamber during removal of the stitches	5	10	0	
Hyphema	1	2	0	
Total flatness of anterior chamber	12	24	1	2
Spontaneous hyphema	0	0	0	0

TABLE 2.—*Immediate Results*

	Av. Day of Removal of Suture	Av. Vision	Astigmatism in the 1st Refraction
Commonly used suture	13.47	0.54 (on av. day 24.24)	1.86 D. (on av. day 24.24)
Subconjunctival suture	7.2	0.58 (on av. day 18.19)	1.32 D. (on av. day 18.94)

observed, a better visual acuity five days sooner, and an astigmatism of 0.5 D. less, also five days sooner, with the use of the subconjunctival suture.

After examination of these results, it can be stated that multiple subconjunctival sutures are to the postoperative course what good sedation and curarization are to the operation. Just as these latter factors result in an extraordinary reduction in operative accidents and make the operation less disagreeable to the patient, so the suture herein described reduces in a large proportion the postoperative accidents and, at the same time, allows the patient to have a much rapider and more comfortable convalescence.

Apartado Aereo 11056.

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Ocular Metastases in Hutchison-Pepper Syndrome

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The purpose of this paper is to report on the involvement of various structures of the eye in a case of Hutchison-Pepper syndrome (neuroblastoma of the adrenal gland with involvement of the liver and the orbit) which underwent spontaneous retrogression. The report seems justified in view of the fact that no reference could be found in the literature in which metastatic deposits were reported in the ocular tissues. It will also add to the literature another case of spontaneous retrogression in a proved case of neuroblastoma of the adrenal gland.

Historical Review

The tumors of the adrenal gland consisting of immature pleuripotential undifferentiated neuroblasts, which are now termed neuroblastoma or sympathicoblastoma, were first described as gliomata by Virchow (1864). Subsequently they were grouped as "round-celled sarcomas" of the adrenal gland or "lymphosarcomas." A review of the previous records shows that many of such recorded tumors are of the nature of neuroblastoma. Possibly Morgan's (1879) case of "sarcoma of the scapula" in an infant 9 weeks old, in which the left adrenal as well as other viscera contained growth and the sarcomatous tissue showed "some parts delicately fibrillated," was a neuroblastoma. Abercrombie (1880) described in a 4-year-old girl "multiple sarcomata of cranial bones" in which there was a tumor beneath the left adrenal with involvement of a chain of lumbar lymph glands and multiple deposits in various parts of skeleton as well as the skull; this was undoubtedly a case of neuroblastoma of the adrenal with metastatic deposits. Parker's (1880) case of congenital "sarcoma of the liver" was in all probability a case of neuroblastoma of the adrenal with secondary involvement of the liver. Dalton (1885) reported a typical case of neuroblastoma of the adrenal gland with metastases in the liver, which he classified as "lymphosarcoma." His case was an infant 6 weeks old, and he described unequivocally the characteristic arrangement of cells in rosette formations in the adrenal tumor; in spite of the fact that the growth in the liver was of huge size as compared with that of the adrenal, Dalton suspected the tumor of "originating in the medulla of the adrenal. . . . The liver affection might then be secondary." The tumors described by Moore (1885) and Chaffey (1885) were also undoubtedly adrenal neuroblastoma.

Marchand (1891) noted the resemblance of this tumor to that of the developing central nervous system. Pepper (1901) described a tumor in a 6-week-old infant with involvement of the liver and right adrenal gland which he called "lymphosarcoma." From his description originated the so-called Pepper syndrome—the syndrome of massive hepatic metastases from adrenal neuroblastoma. Hutchison (1907) reported 10 cases of adrenal tumor with metastases to bones of the skull, 4 of which were his own. He described the condition as the syndrome of "suprarenal sarcoma in children with metastases in the skull"—a syndrome which, in later years, was named after him. These types (Pepper's and Hutchison's) are no longer acceptable, since Farber (1940) and Karsner (1942) showed that the distribution

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of metastatic deposits bears no relation either to the anatomical location of the primary tumor or to its cytological character. Geschickter (1933) and Bergstrom (1937) are of opinion that the two types are indistinguishable pathologically and probably differ in their clinical course only by reason of the age at which they become apparent. Tileston and Wolbach (1908) observed cell rosettes in a tumor which had produced Hutchison's syndrome, but they failed to recognize the origin of the growth.

The true nerve cell character of the tumor was first recognised by Marchand (1891), who noted the likeness of the tissue of the tumor to that of the developing sympathetic ganglia. Wiesel (1905) was very critical of Küster's (1905) contention that the rosettes were of the nature of a glioma and identified them with the *Markballen* of the embryonic adrenal medulla or sympathetic ganglia. Wright (1910), in a beautifully illustrated paper, finally established the identity of the neuroblastoma by comparing the rosettes and parallel bundles of fibrils in the tumors with those seen in embryonic adrenal medulla and sympathetic system. Subsequently Herxheimer (1914), using the Bielchowsky method, showed for the first time that the fibrils in an adrenal neuroblastoma were fine nerve fibers and that they arose as outgrowths of cells.

Origin

It is now established that the neuroblastoma of the adrenal gland arises from the same cells as does the medulla of the adrenal gland, as well as portions of the sympathetic nervous system. The medulla of the adrenal originates from the ectoderm of the primitive neural crest. Two types of cells are found developing from the neural crest, which are called sympathogonia. In the process of differentiation they may either become chromaffin cells of the adrenal medulla or they may form the sympathoblasts which finally become the sympathetic ganglion cells.

It is generally assumed that fully differentiated nerve cells are incapable of multiplication. This tumor, arising from undifferentiated migratory cells, may have its origin in widely varying parts of the body. The adrenal gland accounts for about one-third of all cases and is the most frequent single site of origin of these tumors; the abdominal and pelvic sympathetic chains and associated ganglia account for another one-third, while the remaining one-third arises from cervical and thoracic parts of the sympathetic chains. No significant variation has been observed in the incidence of tumors on the two sides.

Age Incidence

Scott et al. (1933) showed that in 50% of the reported cases the patients had been less than 2 years old and in at least 75% less than 4 years. Gross (1953) showed from his collection that 30% occur in first year of life, 80% within the first five years, and only 20% beyond that age. Of Gross's cases, the youngest patient was 1 day of age and the oldest was 15 years old.

Instances have been reported in which the tumors have been present at birth, causing dystocia. Of late, cases occurring in adolescents and adults have been reported. As it is generally assumed that fully differentiated nerve cells are incapable of multiplication, neuroblastoma cannot, therefore, arise from adult sympathetic or adrenal tissue. To determine the age limit for the possible origin of these tumors, it is important to find out at what period of postnatal life proliferation and differentiation of formative sympathetic and adrenal tissue cease. Weisel (1902) is of opinion that the sympathogonia, from which the adrenal medulla develops, begins to invade the cortex during the eighth week of fetal life and begins to collect centrally; this migration continues possibly until puberty. Theoretically, the neuroblastoma could, therefore, arise at any time prior to 12 years.

Histology

Microscopic examination of these tumors reveals a highly cellular structure consisting

of closely aggregated small rounded or polyhedral cells with scanty ill-defined cytoplasm and each with a single spherical or slightly ovoid nucleus—an appearance like that of lymphocytes. A few larger round cells with vesicular nuclei and some pear-shaped cells resembling spongioblasts can be seen. There are many mitotic figures in the spherical nuclei. All the cells give off delicate processes which unite to form a fibrillar syncytium. Two characteristic features of this tumor are considered to be diagnostic—arrangement of groups of cells in rosette formation and development of neurofibrils.

Kato (1938) is of opinion that this arrangement of cells in rosette formation should better be called a pseudorosette, since there is no central canal. The cells in a well-differentiated rosette are often pear-shaped, with their tail-processes directed centrally to become the young nerve fibers of the center of the rosette.

Landau (1912) has tried to demonstrate the general correlation between the age of clinical appearance of the tumor and the histological differentiation and clinical malignancy. The tumors which are present at birth or appear during infancy—usually those types which produce so-called Pepper's syndrome—consist mostly of diffuse round-celled growth with no rosette formation or very indefinite rosettes and are usually very rapidly fatal, whereas the tumors producing so-called Hutchison's syndrome, which appear a little later, say between 2 and 8 years, though very cellular, frequently show rosettes and are a little less rapidly fatal. Neuroblastomas occurring in adolescents and adults may show a high degree of rosette formation and fibril differentiation and are often of slower growth. Blacklock (1934), however, is of opinion that there are many exceptions to the general correlation between the age of onset and the degree of malignancy and histological differentiation of the tumors.

Metastasis

Neuroblastomas are highly malignant growths with the potentiality of wide and extensive dissemination. Metastasis usually takes place from the primary site in one or all of three ways—by direct extension, through lymphatics, and through blood vessels. In a great majority of cases the primary tumor is so small and symptomless that attention is drawn to the condition only because of massive hepatic enlargement or metastatic deposits in the bones. Some of these metastatic syndromes are so characteristic that they have been given eponyms. Thus Pepper's syndrome indicates great hepatic enlargement due to secondary deposits of neuroblastoma in the liver; Hutchison's syndrome denotes metastatic deposits of neuroblastoma in the skull. Colville and Willis (1933) and subsequently Willis (1940) pointed out that at least some cases of so-called Ewing's syndrome are really metastatic deposits of neuroblastoma in long bones which have escaped recognition.

Metastasis in neuroblastoma may occur in any organ or tissue. Liver may be involved by direct invasion from right-sided adrenal tumor or in true metastasis, or the two may coexist, resulting in massive hepatic enlargement (Richards, 1905; Dunn, 1915; Blacklock, 1934). In infants or young children great hepatic enlargement is often seen (Pepper's syndrome).

Metastases in bones are often very frequent, though they may not be obvious on clinical examination. In Hutchison's syndrome main attention is drawn to the deposits in the skull and orbit, but a careful clinical and radiological examination will often reveal less conspicuous involvement of many other bones.

Hutchison's syndrome is of great interest to ophthalmologists. Redman, Agerty, Barthmaier, and Fisher (1938) collected 275 cases with orbital involvement. Guibor (1942) later increased the figure to 291 since Virchow's original publication in 1864. In a recent survey Portray and Danis (1949) brought the total to 300 cases from the world literature.

Metastases in the orbit. Clark (1939), summarising Bergstrom's review of 200

cases, estimated that approximately 25% of neuroblastomas showed metastatic deposits in the orbit and skull and that the earliest manifestations were ecchymosis of the lids or exophthalmos or both. The condition was usually unilateral and occurred in children from 1 to 15 years of age. X-ray of the skull revealed a firm granular type of osteoporosis produced by multiple metastatic foci with resorption. The growths were situated on the inner and outer tables of the skull.

Early deposits of neuroblastoma in bones appear as soft white nodules in the medulla, which, later on, become diffuse and spread into the marrow spaces and Haversian canals and reach the subperiosteal tissue. These appear as fusiform swellings around ribs and long bones or plaque-like bosses on the flat bones. In the later stages these deposits may spread very extensively, producing patchy rarefaction of the medullary bone. They erode the cortical surface and, breaking through the periosteum, spread irregularly into the surrounding soft tissue.

Metastases in other tissues, such as lymph nodes, lungs, kidney, spleen, pancreas, and ovary, are frequently found. Lymph nodes adjacent to the primary growth are first affected, and subsequently, more distant groups. Clinical enlargement of these nodes seldom appears until a late stage of the disease.

Spontaneous Retrogression

While it is true that neoplasms, benign or malignant, grow without interruption and indefinitely, spontaneous cessation of growth and retrogressive changes are sometimes seen, more frequently in benign than in malignant growths. Very rare cases of spontaneous disappearance of proved malignant growths such as mammary carcinoma, ovarian growths, and malignant melanoma have been reported. Gaylord and Clowes (1906), Strauss (1927), Ewing (1940), and Willis (1952) have given very interesting reviews on the subject. Duke-Elder (1940) cites 11 cases of spontaneous retrogression in retinoblastoma, a tumor histologically allied to neuroblastoma of the adrenal.

Spontaneous retrogression of neuroblastoma of the adrenal has been reported in three cases without any specific treatment by Gross (1953), after x-ray therapy (Lehman, 1952), and by transformation into ganglioneuroma (Cushing and Wolbach, 1927).

Clinical Manifestations

Neuroblastoma of the adrenal is primarily a condition of infancy and childhood, occurring most frequently before the age of 5 years, though it has been known to occur in adults as well. It occurs equally in the two sexes.

As the primary tumor may arise from many different sites, the presenting complaint is necessarily variable, and, unless one is on the lookout, the diagnosis may be entirely misplaced. The initial complaint may be abdominal swelling, proptosis, ecchymosis of the lids, anuria, nervous disorder, or bony swellings. General nonspecific findings of increasing pallor, anemia, progressive loss of weight, and listlessness are usually present. The primary tumor may not be evident, and the symptoms and signs may result from metastases alone. Headache, nausea, vomiting, papilledema, separation of suture lines, and hydrocephalus may result from increased intracranial pressure due to metastases in the skull; proptosis, ecchymosis of the upper eyelid, and optic atrophy may be seen with retrobulbar involvement.

Blood examination may reveal low red blood cell count. Urinalysis may show erythrocytes if the renal pelvis has been invaded. Straight x-ray films of the abdomen may show an area of increased density in the region of the tumor. Radiological evidence of calcification above the kidney region is an extremely important clinical aid in diagnosis. X-rays of bones may show skeletal metastases. Radiating spicules or bony resorption may be evident. A pyelogram may show downward and lateral displacement of the homolateral kidney.

Clinically Hutchison's tumor appears in the orbit of infants and young children, appearing first on the side corresponding to the affected adrenal. The orbital involvement, however, may be bilateral. It usually occurs in children between 2 and 3 years of age and is seldom seen in those above the age of 10. The first localizing signs of orbital involvement are ecchymoses of the lids and proptosis. The proptosis may be very rapid and extreme, and the whole of the orbital cavity may be filled up by the tumor mass encroaching upon it through both the superior orbital fissure and the optic foramen (Seefelder, 1923). Premonitory symptoms are usually vague. Other secondary growths soon appear on the surface of the skull, particularly in the temporal fossa. Marked cachexia, secondary anemia, low-grade fever, loss of weight, loss of appetite, and very rapid debility usually follow in rapid strides before death intervenes in the course of a few months. It is very important to keep in mind that orbital involvement may be the sole evidence of the parent tumor, which may be discovered only at autopsy and sometimes not even then.

Prognosis

In the past most authors found a very poor prognosis after a diagnosis of neuroblastoma was made. Blacklock (1934) estimated average duration of life to be between 8 and 9 weeks; Doub (1937) reported three patients who lived an average of 4 1/3 months; Lewis and Geschickter (1934) found the average duration of life to be 6 months after diagnosis; Lehman (1952) reported a patient alive 15 years after diagnosis. There are increasing evidences from reports of Roussy (1941), Wyatt and Farber (1941), Wittenborg (1950), and others to moderate a little the hopeless prognosis of the previous writers. Beck and Howard (1951), in a review of 475 cases, found 47 as "cures," or about 10% of the total number. There must be many other cases that have not been reported or that have been lost sight of. Gross (1953) broke down his collections into two groups: the first group before 1940 and the second group from 1940 through 1947. He showed an encouraging rise in the three-year cures, from 19% to 29%—an increase which he attributes to improved operative technique and more thorough use of x-ray irradiation. Koop and his co-workers (1955) have reported one of the highest survival rates—31% for infants surviving 14 months or longer after diagnosis.

Report of a Case

A boy of 12 years was brought to the ophthalmic outpatient department of the Nilratan Sircar Hospital, Calcutta, on May

Fig. 1.—Photographs of the patient just after admission, on May 8, 1956.

2, 1956, for pain, proptosis, and chemosis of the right eye and a big swelling on the left side of the face. History revealed that about a month previously the swelling on the jaw appeared, which had been increasing since then, but, as it did not cause much disability, the patient did not consult anybody regarding his ailment. The ocular condition developed about 10 days after the swelling on the jaw appeared.

Examination of the right eye revealed a hard fixed swelling at the lateral aspect of the superior orbital margin encroaching onto the upper eyelid; the conjunctiva was a little chemosed at the upper part; cornea, pupil, lens, and intraocular pressure were normal; there was proptosis, the eye being directed forwards about 4 mm.; movements of the eye were not limited except for a little restriction of upward movement; vision was 2/60; examination of the fundus showed slight edema and hyperemia of the optic disc and congestion of the retinal veins.

In the left eye nothing abnormal was detected. Vision was 6/6. The fundus appeared healthy.

Swelling on the Jaw on the Left Side.—A hard swelling about the size of an orange, with well-defined margins, overlying the parotid region, was seen. The overlying skin was stretched but not fixed to the mass. Local temperature was raised slightly, with a few prominent veins overlying the swelling. The swelling was fixed to the bone. There was difficulty in opening and closing the mouth; articulation and speech were impaired.

General Examination.—A fullness was noticed in the right hypochondriac and the epigastric regions. The liver was enlarged 4 finger breadths and was firm. A firm lump was palpated in the epigastric region, and a firm rounded swelling, in the right renal region. No other mass was detected in any other place.

The condition was diagnosed as Hutchison-Pepper syndrome, and the patient was admitted the same day (May 2, 1956) under the care of one of us (B. K. D. G.).

Progress of the Case.—From the day of his admission the condition of the patient gradually became worse. He became listless, marasmic, and apathetic and refused to take his meals. On May 7, 1956, signs of portal hypertension appeared. There was extensor plantar response to the Babinsky test, showing involvement of spinal column as well. The liver mass, jaw swelling, and lump in the renal region together with the proptosis of the right eye were gradually increasing. The conjunctiva became more chemosed; proptosis caused ulceration of the cornea, which eventually sloughed out completely, with extrusion of the lens. The patient became very anemic and edema of the feet developed.

On June 14, 1956, a palpable swelling about 4×3.5 cm. developed on the left side of the vertebral column over the ribs in the middorsal region. The skin was free, and there was no sign of inflammation. The deep cervical nodes on the left side of the neck were now all enlarged, and the patient could hardly open his mouth. He was fed entirely with liquids, as solid food could not be taken.

Regression.—On June 26, 1956, a sudden change in the whole picture was noticed: The lump on the back was noticed to have disappeared; the lumps on the jaw and liver regions were felt to become soft and regressed to a certain extent; the enlarged hard cervical glands had become soft; the proptosis was becoming reduced, and the patient now started talking and taking his meals. From this time on the patient showed signs of improvement in his general condition; he gained strength and was able to move out of his bed; edema of the feet disappeared; swelling on the jaw, liver, and kidney regions regressed totally except a small nodule in the cheek. There was nothing more unusual about him to be noticed, and recordings of his weight showed a gradual increase. However, the nodule on the cheek, which had almost totally disappeared, began to increase from July 28, 1956, but to a very slight extent. On Sept. 22, 1956, another

Fig. 2.—Photographs after regression, taken on July 12, 1956.

two small nodules were noticed over the jaw on the left side.

Subsequent Development.—The patient was progressing fairly well. On Sept. 22, 1956, a small nodule was detected on the left side of the cheek. Two other nodules appeared some days later at the same site. On Oct. 29, 1956, a biopsy was done which showed the same malignant characteristics as were previously found. Thereafter, the patient developed multiple swellings all over the body. A lump was detected on the medial side of the vertebral border of the right scapula, and a fairly big swelling was detected at the posteromedial aspect of the left thigh in the muscle. Toward the end of November, 1956, an enormous swelling developed on the left side of the face, extending over the nape of the neck, and the patient's condition deteriorated gradually. He had now no control of the sphincter, and there was constant dribbling of urine. Edema now extended to the whole of the face and the scalp. Subsequently, basal congestion developed on both sides, and he died on Jan. 12, 1957.

Fig. 3.—X-ray of the mandible, showing bony resorption at the angle.

Investigations.—1. Straight x-ray films of all the bones were made on May 3, 1956. The left mandible showed osteolytic reaction. No change was found in the bony wall of the right orbit. No other bones showed any abnormality. Two further x-rays were made of the right orbit, with negative findings.

2. Perirenal pneumography was done on May 8, 1956, which showed a tumor mass in the right kidney region. No calcification was seen.

3. Presacral pneumography with intravenous pyelography was done on May 16, 1956, which showed that the kidney was free of tumor mass and the calyces were normal.

4. Biopsy of the mass on the jaw was done on May 10, 1956. The section showed closely aggregated small rounded cells with

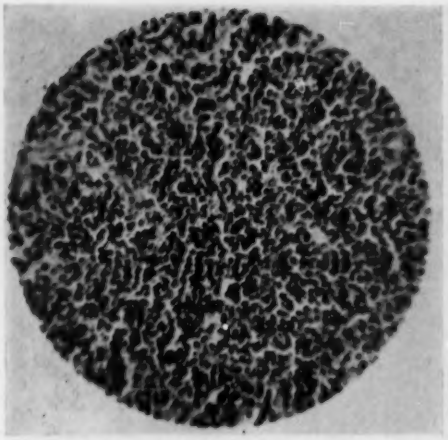


Fig. 4.—Biopsy specimen from the mass on the jaw. Photomicrograph showing closely aggregated small rounded cells with deep-staining nuclei. There are many mitotic figures. Rosette formations are present. Hematoxylin and eosin; reduced slightly from mag. × 60.

deep-staining nuclei and very scanty ill-defined cytoplasm. There were many mitotic figures. Groups of cells in rosette formations were seen. The diagnosis of neuroblastoma was confirmed.

5. The right eye was enucleated on July 13, 1956. The iris, ciliary body, ciliary processes, choroid, sclera, and optic nerve were found to be infiltrated with the same type of cells as were seen in the histological

Fig. 5.—High-power magnification of the biopsy specimen from the jaw. Typical rosettes are seen. Hematoxylin and eosin; reduced slightly from mag. × 180.

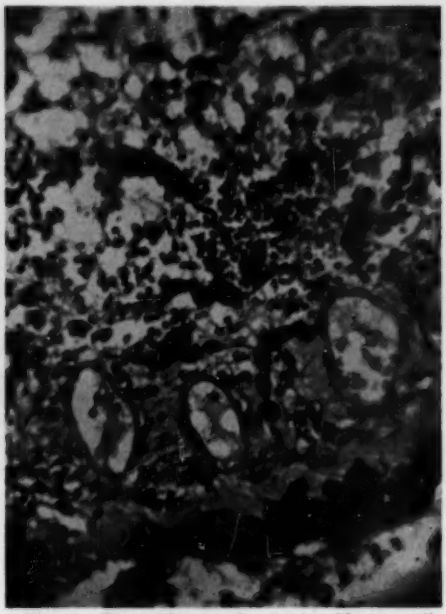


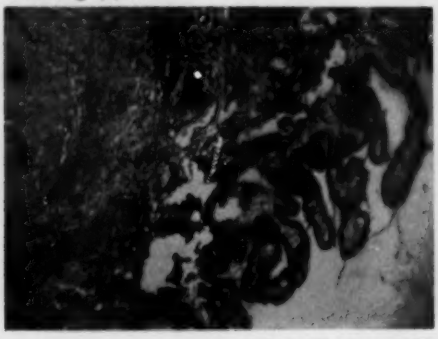
Fig. 6.—Photomicrograph of iris. Hematoxylin and eosin; × 180.

section of the soft tissue of the jaw. In addition, larger rounded cells with vesicular nuclei and pear-shaped cells with tail-processes were seen. There were many mitotic figures, and rosette formations were seen.

6. Blood examination report: Hb., 10 gm. per 100 ml.; RBC, 3,200,000; total WBC, 7300 per cubic millimeter; differential count: polymorphonuclear cells, 64%; lymphocytes, 34%; eosinophils, 2%; basophils, 0%.

7. Urine: Total quantity in 24 hours, 1560 ml.; 17-ketosteroid estimation, 1.6 mg.

Fig. 7.—Photomicrograph of ciliary processes (low power). Hematoxylin and eosin; reduced from mag. × 40.



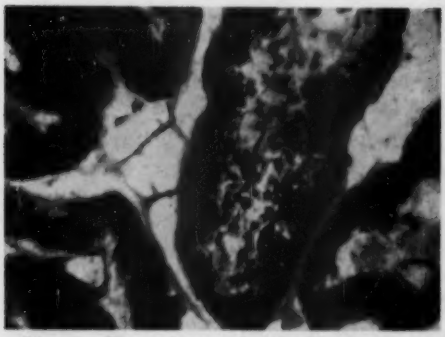


Fig. 8.—Photomicrograph of ciliary processes (high power). Hematoxylin and eosin; reduced from mag. × 1080.

in 24 hours; ketogenic steroid, 2.24 mg. in 24 hours.

8. Weight showed a gradual improvement, as follows:

Date	Weight, Lb.
17/7/56	48
23/7/56	52
31/7/56	54
13/8/56	58
26/8/56	60
2/9/56	60
11/9/56	62
29/9/56	64

Fig. 9.—Photomicrograph of the choroid. Hematoxylin and eosin; × 180.

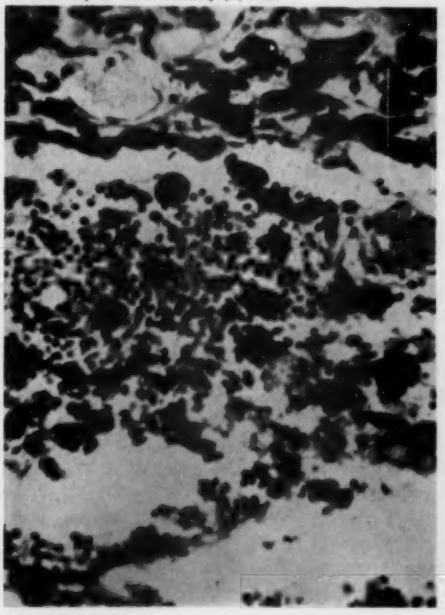


Fig. 10.—Photomicrograph of the sclera. Hematoxylin and eosin; reduced from mag. × 180.

Comment

Neuroblastoma of the adrenal with involvement of the liver and the orbit and other metastatic deposits, though uncommon, is not a rarity, if one is on the lookout in cases of unilaterial proptosis occurring in infants and children. The case reported here was so bad and at the same time so interesting that the patient was admitted immediately. The condition was deteriorating so fast that none of us could hope that he would last more than a fortnight. He was kept constantly on meperidine hydrochloride (Pethidine) and other sedatives and was given intravenous dextrose daily during the period when it was not possible for him to take any food whatsoever. The question of blood transfusion was considered, but because of the very bad condition of the patient the idea was given up.

Fig. 11.—Photomicrograph of the optic nerve. Hematoxylin and eosin; reduced from mag. × 40.

Fig. 12.—Photomicrograph of the optic nerve. Hematoxylin and eosin; × 1080.

When the cornea sloughed out and proptosis regressed, it was considered worth while to enucleate the eye instead of eviscerating it, to see if any signs of metastatic deposits could be found in the interior of the eye. All that could be found in the literature regarding the causation of proptosis was infiltration of the retrobulbar tissue with metastatic deposits and deposits in the skull bones. In the case just described, metastatic deposits were found in the vascular coats of the eye, sclera, and optic nerve. No sign of metastasis was detected in the retina. As the cornea was sloughed out, it could not be examined.

It was remarkable at what pace retrogression proceeded. The appearance of nodules on the left sides of the jaw after they had almost totally disappeared makes the case more interesting.

Summary

A case of neuroblastoma of the right adrenal with massive hepatic involvement, orbital metastases, and metastatic deposits in other regions is presented (Hutchison-Pepper syndrome).

The history, origin, pathology, and clinical manifestations of the condition are described.

The case spontaneously retrogressed without any treatment whatsoever (except intravenous dextrose).

Metastatic deposits were found in the iris, ciliary body, ciliary processes, choroid, sclera, and optic nerve of the proptosed eye. No mention of involvement of structures of the eye in neuroblastoma of the adrenal could be found in the literature.

The Superintendent, Nilratan Sircar Hospital, Calcutta, gave permission to publish this case; Dr. D. Sarkar, Radiologist of the Nilratan Sircar Hospital, took about 35 x-rays; Dr. R. Datta Choudhury, Chittaranjan Seva Sadan, Calcutta, made the biopsy report from the swelling on the jaw; Dr. H. Chakravarty made estimations of ketosteroids, and K. Das took all the photomicrographs.

Nilratan Sircar Medical College.

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Glutathione Protection in X-Irradiated Eyes

A Preliminary Report on Enzymatic and Clinical Changes

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In recent years the protective action of sulfhydryl-containing compounds on changes induced by ionizing radiations has been comprehensively reported. After the early reports by Patt et al. (1949),[1] Chapman et al. (1949),[2] and Barron and Dickman (1949),[3] information accumulated that sulfhydryl-containing compounds act as competitive acceptors for certain injurious products, such as hydroxyl and perhydroxyl radicals, formed in irradiation of the tissue water in the presence of oxygen. It seems probable that some protection may be obtained in any tissue, provided that a sufficient sulfhydryl concentration can be established. The actual degree of protection cannot be anticipated until sufficient experimental evidence is available to determine whether the action of the drug can be interpreted entirely on the basis of a reduction in the initial amount of radiation damage.

Glutathione was selected for the present experiments because mammalian tissues all contain appreciable amounts of glutathione, indicating that regulatory mechanisms for glutathione exist in the organism. In addition, the role of glutathione in enzymatic reactivation [4,5] and cellular metabolism [4,6] further indicated its selection. Voegtlin [6] suggested that the reducing action of glutathione would maintain the activity of the enzymes that catalyze protein synthesis and thereby favorably influence growth. It has also been shown that embryonic and some cancer tissues contain larger amounts of glutathione than normal tissues.[7]

In separate reports, Eichel and Swanson [8,9] have presented data concerning the quantitative estimation of succinic dehydrogenase, diphosphopyridine nucleotide (DPN) cytochrome C reductase, cytochrome oxidase, glucose-6-PO_4 dehydrogenase, pyruvic reductase, and catalase in normal rabbit tissues.

Glutathione having been selected for our initial work with SH compounds in ocular tissues, experiments were designed to test its effect on irradiated animals with respect to (*a*) enzyme changes and (*b*) clinical effects.

Experimental Procedure

Animals.—New Zealand white male rabbits approximately 6 months old and ranging in weight between 6 and 7 lb. (2.7 and 3 kg.) were used. They were housed in individual cages and maintained on an ad libitum diet of Purina rabbit chow and water.

The animals were grouped as follows: Group A consisted of normal animals; Group B consisted of irradiated animals; Group C consisted of animals which were irradiated and treated with glutathione a few minutes prior to irradiation. Group D received only glutathione. Ten animals were included in each group.

Irradiation.—All irradiated rabbits received x-ray irradiation in a single exposure limited to the head. Three different doses were employed: 800 r, 2240 r and 6000 r (±5%).

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From the Department of Pathology, Physiological Chemistry Section, and the Department of Ophthalmology, School of Aviation Medicine, U. S. A. F., Randolph Air Force Base, Texas.

The animals to be irradiated were bound to a Y-shaped board. The head was immobilized at a 45 degree angle to the longitudinal axis of the board with gauze. A Picker deep therapy x-ray unit was used as the source. The rate of irradiation was measured in air and in the eye of the rabbit with a Victoreen chamber dosimeter. The measurements in air were made 23 cm. from the source; the measurements in the eye were made by placing the dosimeter in the vitreous space of animals killed (with intravenous injection of pentobarbital [Nembutal]) after they were placed in position for irradiation.

Irradiation parameters were the following: 260 kv.; 18 ma.; source-target distance 23 cm.; irradiation rate in the vitreous space of 310 r per minute (average of six measurements in each eye); dose approximately 6000 r, 2240 r, and 800 r; irradiation rate in air 350 r per minute (average of six measurements). The inherent filtration of the x-ray tube was equivalent to 0.25 mm. of copper; also a filter of 1 mm. of aluminum and 0.5 mm. of copper was used. The dose recorded in the vitreous space is used in reporting this work, as it is more nearly the same as the dose received by the ocular tissues selected.

Glutathione.—All glutathione-treated rabbits received a single injection immediately preceding irradiation. Each rabbit was given 4000 mg/Kg. body weight intravenously in the marginal ear vein.

Clinical Examinations.—All rabbits were examined with a Zeiss Opton slit lamp and May type of ophthalmoscope several days preceding irradiation and also before they were killed for enzyme determination. Examinations were conducted in such a way that the examiner did not know at the time whether he was examining an irradiated or an irradiated-protected animal.

Handling of Tissues.—The rabbits were killed by decapitation. The retina, combined iris and ciliary body, cornea, and conjunctiva were taken from the right eye, whereas the combined lens capsule and epithelium from right and left eyes was required to yield a sufficiently large homogenate sample for analysis. The wet weights of the tissues were determined with a Meteler gramatic balance, and they were immediately disintegrated in small Ten Broeck glass homogenizers with ice cold 0.05 M KH_2PO_4-$NaHPO_4$ buffer, pH 7.4, to yield a final 1:50 (weight/volume) homogenate dilution.

Microprotein Method.—A modification [8] of the method of Kabat and Mayer [10] employing the Folin-Ciocalteau phenol reagent was used.

Enzyme Analyses.—These determinations were made with a Beckman Model DU Spectrophotometer. The enzyme assays for succinic dehydrogenase, cytochrome oxidase, and glucose-6-PO_4 dehydrogenase were modified slightly.[9]

Results

The following clinical observations were made in various tissues of the eye after exposure to ionizing radiation to given doses with and without glutathione treatment (Table 1).

Conjunctiva.—Twenty-four and forty-eight hours after irradiation the conjunctiva and nictitating membrane were hyperemic in the animals which received 2240 r and 6000 r. The hyperemia was more pronounced and more often seen in the animals which received 6000 r. Edema of the conjunctiva with some secretion was noted in a few animals irradiated with 2240 r and in more animals and to a higher degree in those irradiated with 6000 r.

In the animals treated with glutathione and irradiated the following findings were noted. In animals irradiated with 2240 r and 6000 r, hyperemia of the conjunctiva was seen rarely and at a minimal level (two animals seen with 2240 r and one animal with 6000 r). Edema of the conjunctiva was not seen in the group irradiated with 2240 r and treated, and it was seen in only one case with 6000 r.

Cornea.—Corneal opacity and edema were seen in some animals irradiated with 2240 r and in most of the animals irradiated with 6000 r.

TABLE 1.—*Clinical Findings in X-Irradiated Rabbit Eyes, With and Without Glutathione (GSH)**

Eye Tissue	Clinical Condition Observed†	800 r				2,240 r				6,000 r			
		24 Hr.		48 Hr.		24 Hr.		48 Hr.		24 Hr.		48 Hr.	
		Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH
Conjunctiva	Hyperemia, edema	‡				8 3	2	7 1	2	10 7	1	9 8	0 1
Cornea	Opacity, edema					3 5		2 7		9 8		10 9	
Anterior chamber	Flare 1+ 2+ 3+ 4+	7	2	8	1	2 4 4	6	3 3 4	8	5 5	7 3	4 6	4
	Cells 1+ 2+ 3+ 4+	4		5		7 2 1	3	8 2	2	9 1	8	8 2	5 3
Iris & ciliary body	Hyperemia, hemorrhage	9 9	3 2	8 7	2 1	10 10	8 7	10 10	9 8	10 10	10 10	10 10	10 10
Lens	Suture lines					10	2	8	2	10	3	10	2
Vitreous body	Cells 1+ 2+	2		1		3	1	4		5	2	3	2
Retina	Edema, hemorrhage					3 2		4 1		8 1		8 1	

* Numbers of rabbits (10 animals in each group) by level of radiation and time after exposure.
† Combined observation of right and left eyes for each animal.
‡ All blank entries indicate that examinations were conducted and no abnormalities were observed.

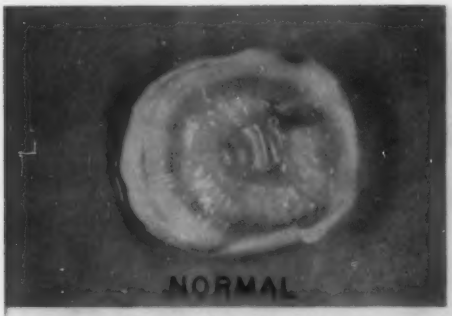

Fig. 1.—Normal animal.

Fig. 2.—Animal injected with glutathione only; killed 24 hours after injection.

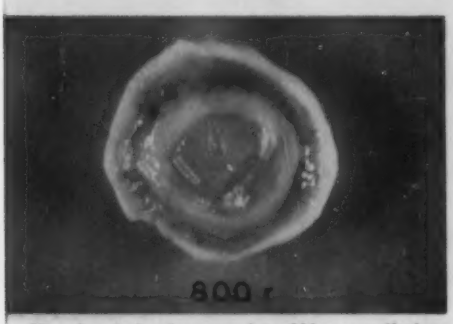

Fig. 3.—Animal exposed to 800 r x-radiation; killed 24 hours after exposure.

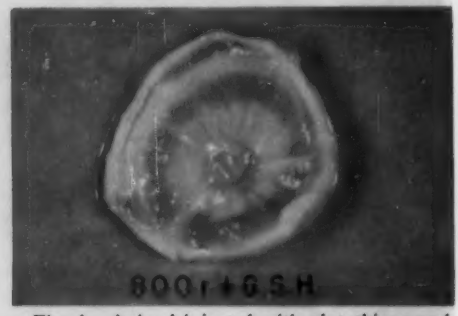

Fig. 4.—Animal injected with glutathione and exposed to 800 r x-radiation; killed 24 hours after exposure.

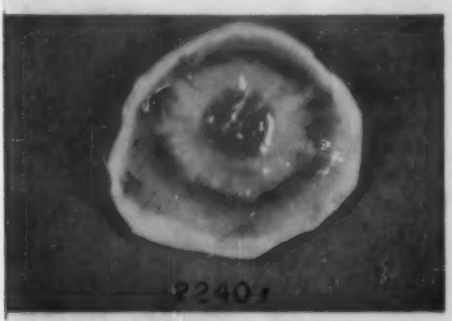

Fig. 5.—Animal exposed to 2240 r x-radiation; killed 24 hours after exposure.

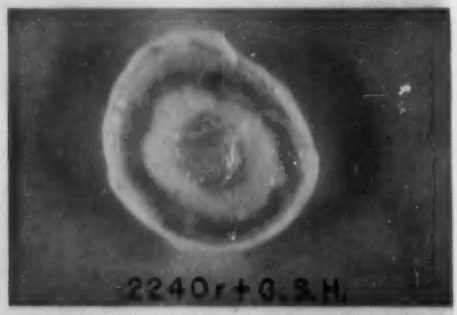

Fig. 6.—Animal injected with glutathione and exposed to 2240 r x-radiation; killed 24 hours after exposure.

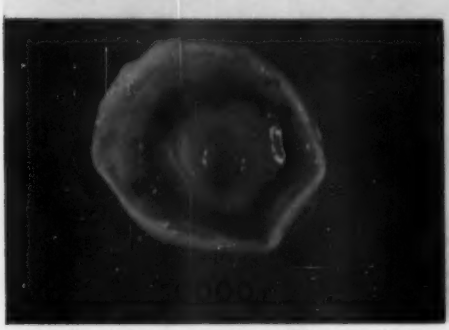

Fig. 7.—Animal exposed to 6000 r x-radiation; killed 24 hours after exposure.

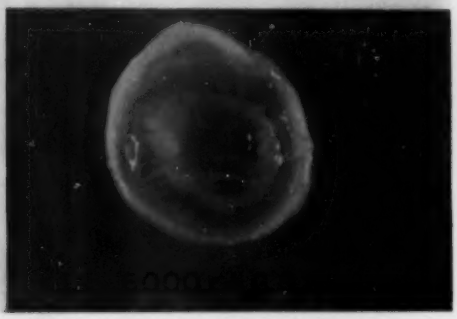

Fig. 8.—Animal injected with glutathione and exposed to 6000 r x-radiation; killed 24 hours after exposure.

None of the animals treated with glutathione and irradiated at 2240 and 6000 r showed corneal opacity and edema.

Anterior Chamber.—Tyndall effect, or flare, was often observed. It was scored on a four-point scale.

A moderate number of animals irradiated with 800 r showed flare no higher than 1+. In the group irradiated with 2240 r, all animals showed flare from 1+ to 3+. All animals irradiated with 6000 r had flare from 3+ to 4+. One such animal had a heavy gelatinous mass filling the anterior chamber completely.

The animals treated with glutathione and irradiated exhibited flare more rarely and to a lesser degree. A few animals in the group irradiated with 800 r had only a minimal flare. In the group irradiated with 2240 r, a considerable number had flare, but no greater than 1+. In the group irradiated with 6000 r, a considerable number had 1+ and few had 2+ flare, none higher.

In the animals which were irradiated without prior glutathione treatment, the number of cells found in the anterior chamber varied with the exposure level; however, the animals which were treated with glutathione and irradiated showed at each level a considerably smaller number of cells.

Cells precipitated on the anterior lens capsule varied in the untreated animals with the level of exposure. In the animals treated with glutathione and irradiated, no cells were found precipitated on the anterior lens capsule.

Iris and Ciliary Body.—Hyperemia was observed to vary in degree with the level of radiation.

In the animals treated with glutathione and irradiated, iris hyperemia was noted rarely in the 800 r group.

On the dorsal surface of the iris and ciliary body radial flame-shaped hemorrhages were noted in all irradiated animals, varying in degree with the level of radiation (Figs. 1-8). These hemorrhages were seen during dissection and were often easily discernible through the unpigmented iris during slit-lamp examinations.

These hemorrhages were seen to a conspicuously smaller extent, varying from none to scattered small petechial hemorrhages, in those animals treated with glutathione and irradiated.

Lens.—No conspicuous opacities or vacuoles were found (the animals were killed at 24 and 48 hours after irradiation).

The sutures of the lenses varied widely before irradiation, and in some animals they were hardly visible whereas they were somewhat conspicuous in others. After irradiation the sutures became conspicuous to very prominent, especially in the animals irradiated with 2240 and 6000 r.

This increasing conspicuousness of the sutures was rarely seen in the animals which were treated with glutathione and irradiated.

Vitreous Body.—In the vitreous body an increase in the number of cells was observed to vary with the level of radiation.

This increase was observed to a less degree in those animals which were treated with glutathione and irradiated.

Retina.—The ophthalmoscopic examination was at times very difficult or impossible in irradiated animals because of loss of transparency of the media. In the animals in which the fundus could be seen, edema was observed in the groups irradiated with 2240 and 6000 r. Hemorrhages were observed only very rarely.

Edema of the retina was not observed in animals that were treated with glutathione and irradiated.

Succinic Dehydrogenase.—Activities in the retina decreased at 2240 and 6000 r, whereas the lens capsule activity did not differ significantly (Fig. 9 and Table 2) and was essentially the same as in the normal animal. In the iris a diminished activity was observed after irradiation with 800, 2240, and 6000 r. However, with the exception of iris at the 2240 r level, it was possible to demonstrate recovery of the enzyme if the animals were treated with glutathione before irradiation.

Cytochrome Oxidase.—Following irradiation no decrease in cytochrome oxidase was observed in the retina. Lens capsule showed

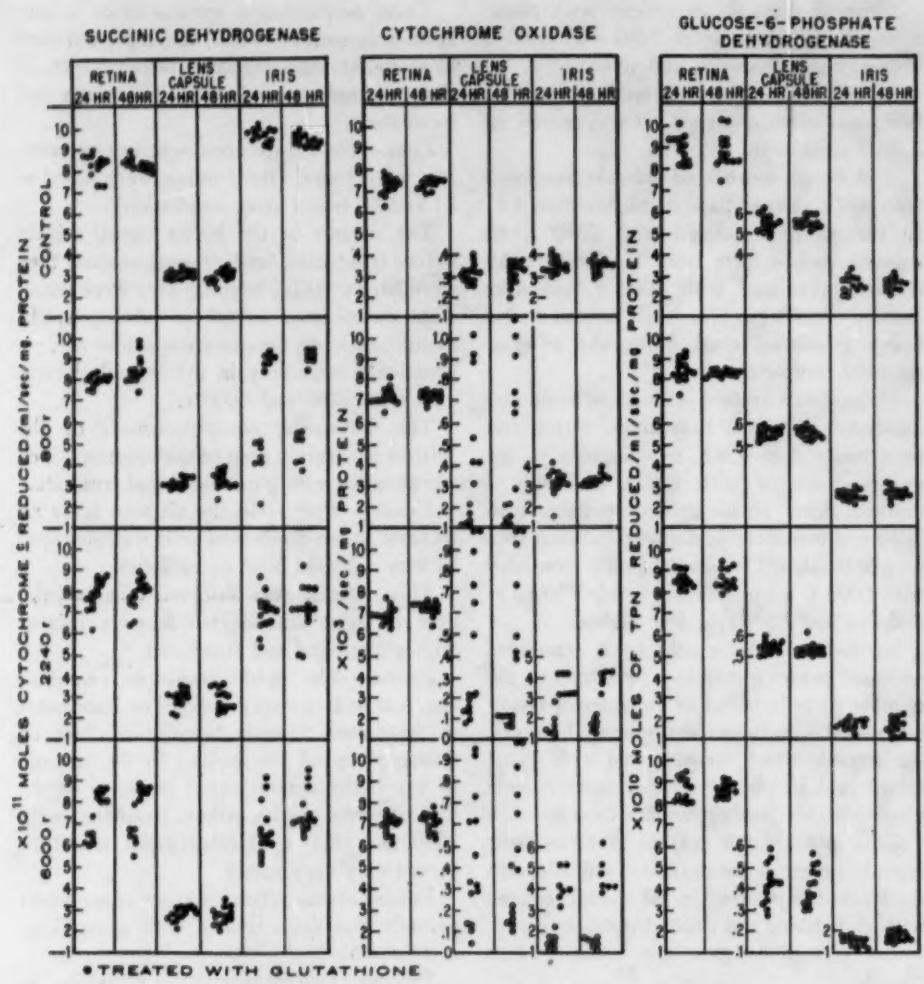

Fig. 9.—The individual results of seven animals for each group.

a fall in activity notably at 800 and 2240 r 24 and 48 hours after irradiation (Fig. 9 and Table 3). When compared with controls, a significant decrease was seen in the iris and ciliary body of animals irradiated with 2240 r and 6000 r.

If the animals were treated with glutathione before irradiation, there was no decrease in enzymatic activity in lens or the combined iris and ciliary body, and in the metabolism of these tissues there appears to be an increase in cytochrome oxidase activity.

Glucose-6-Phosphate Dehydrogenase.—No significant inhibition was observed in the retina of the irradiated animals at all three dose levels (Fig. 9 and Table 4). A very marked fall in activity was observed in lenses irradiated with 6000 r. In the iris and ciliary body, an obvious inhibition was found at the 2240 r and 6000 r levels.

In the animals irradiated and treated with glutathione a protective effect was seen in the lens, whereas no alteration in recovery in the enzyme activity of the iris was observed 48 hours after irradiation.

TABLE 2.—*Succinic Dehydrogenase* *

Amount of Irradiation	Retina				Lens				Iris			
	24 Hr.		48 Hr.		24 Hr.		48 Hr.		24 Hr.		48 Hr.	
	Without†	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH
Control	8.55±0.16	8.00±0.23	8.44±0.10	8.05±0.08	2.94±0.04	3.14±0.06	2.83±0.06	3.05±0.06	9.71±0.09	9.39±0.15	9.45±0.10	9.21±0.04
800 r	7.90±0.11	8.14±0.04	8.11±0.13	8.78±0.31	3.01±0.05	3.25±0.08	3.34±0.18	3.31±0.11	4.23±0.40	8.92±0.04	4.73±0.28	9.03±0.10
2,240 r	7.24±0.24	8.40±0.10	7.32±0.23	8.33±0.12	2.74±0.17	3.10±0.10	3.05±0.22	2.82±0.17	6.84±0.43	7.11±0.21	7.21±0.62	7.33±0.24
6,000 r	6.47±0.17	8.34±0.12	6.68±0.31	8.50±0.11	2.61±0.12	2.99±0.04	2.60±0.13	2.88±0.11	6.26±0.36	7.15±0.48	6.95±0.18	7.94±0.40

* $X10^{11}$ moles cytochrome C reduced/ml/second/mg. protein.
† Average of seven animals ± standard error of mean.

TABLE 3.—*Cytochrome Oxidase* *

Amount of Irradiation	Retina				Lens				Iris			
	24 Hr.		48 Hr.		24 Hr.		48 Hr.		24 Hr.		48 Hr.	
	Without†	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH
Control	7.07±0.23	7.30±0.11	7.22±0.09	7.41±0.10	0.295±0.007	0.319±0.02	0.287±0.02	0.327±0.01	3.39±0.16	3.41±0.09	3.41±0.12	3.38±0.09
800 r	7.10±0.09	7.36±0.16	7.34±0.14	7.24±0.06	0.137±0.01	0.638±0.11	0.162±0.01	0.910±0.21	3.05±0.31	3.23±0.09	3.17±0.05	3.40±0.09
2,240 r	6.90±0.17	7.02±0.13	7.13±0.12	7.09±0.11	0.141±0.02	0.723±0.12	0.098±0.01	0.737±0.12	1.64±0.24	3.52±0.19	1.68±0.11	4.07±0.24
6,000 r	7.04±0.16	6.94±0.17	7.10±0.13	7.20±0.17	0.236±0.07	0.619±0.11	0.191±0.04	0.846±0.16	1.42±0.43	4.14±0.28	1.50±0.10	4.61±0.30

* $X10^{4}$/second/mg. protein.
† Average of seven animals ± standard error of mean.

TABLE 4.—*Glucose-6-PO_4 Dehydrogenase* *

Amount of Irradiation	Retina				Lens				Iris			
	24 Hr.		48 Hr.		24 Hr.		48 Hr.		24 Hr.		48 Hr.	
	Without†	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH	Without	With GSH
Control	9.21±0.21	8.58±0.20	8.81±0.33	8.96±0.25	0.556±0.01	0.536±0.01	0.556±0.008	0.548±0.01	2.81±0.14	2.75±0.13	2.81±0.12	2.74±0.09
800 r	8.40±0.23	8.60±0.17	8.32±0.05	8.38±0.07	0.558±0.01	0.552±0.01	0.568±0.01	0.539±0.01	2.58±0.11	2.59±0.08	2.76±0.13	2.69±0.03
2,240 r	8.68±0.10	8.58±0.20	8.65±0.10	8.62±0.16	0.541±0.01	0.541±0.01	0.539±0.01	0.525±0.003	1.82±0.03	1.80±0.08	1.69±0.11	1.73±0.13
6,000 r	8.68±0.23	8.73±0.18	8.65±0.12	9.03±0.13	0.375±0.03	0.481±0.03	0.356±0.02	0.487±0.02	1.51±0.09	1.75±0.08	1.88±0.05	1.86±0.07

* $X10^{13}$ moles of triphosphopyridine nucleotide reduced/ml/second/mg. protein.
† Average of seven animals ± standard error of mean.

Comment

The data presented here suggest that no significant inhibition was obtained with cytochrome oxidase and glucose-6-PO_4 dehydrogenase in retinal tissue homogenates for all three levels of irradiation.

Retina, lens capsule, and epithelium revealed some alterations in succinic dehydrogenase, cytochrome oxidase, and glucose-6-PO_4 dehydrogenase activity at the 800, 2240, and 6000 r levels. However, the injection of glutathione before the irradiation of the animals produced a "reactivation" of these enzymes, thus enhancing regenerative mechanisms. It may be implied, therefore, that the degree of protection by glutathione depends on the dose that is injected and the amount of radiation given.

The iris and ciliary body were undoubtedly the most severely affected tissues of all the ocular structures studied. The most consistent findings were hemorrhages and enzyme inhibition, varying with the level of radiation, being much more pronounced at the higher doses of radiation.

There is as yet no unanimity of opinion about the mechanism of the hemorrhages in iris and ciliary body. It is possible that several factors are involved, including increased capillary permeability combined with decreased clotting of the blood and, perhaps, a hemolytic factor.[11-13]

The protective effect of glutathione is evident in reducing the severity of the hemorrhages. There was no inhibition in enzyme activity of succinic dehydrogenase and cytochrome oxidase, and in the latter there appears even to be an increase in activity. An explanation for this latter finding is not available at present. The lack of reactivation of glucose-6-PO_4 dehydrogenase at 24 and 48 hours after irradiation may demonstrate definitely that inhibition of this enzyme by x-irradiation may be correlated with hemorrhage affecting tissue metabolism along with the oxidation of the sulfhydryl groups of the protein.

The most successful protective substances are those which depend on the reduction of oxygen tension at the time of irradiation or on the interruption of free radical chain reactions. Because they are capable of reducing the disulphide to the SH form, some hope of reversing the damage was entertained. It may be that they, too, maintain the integrity of various enzymes by acting as free radical acceptors.

This report is preliminary. Experiments are being continued at different hours after irradiation. A long-term study is also being made on animals irradiated with 800 r with and without glutathione protection for survival and resistance to cataract.

Sufficient enzyme data on cornea and conjunctiva are not available at this time.

Summary

A preliminary investigation has been made on clinical and enzymatic changes in rabbit eyes after x-irradiation alone and after x-irradiation preceded by treatment with glutathione.

Conjunctiva, cornea, anterior chamber, iris and ciliary body, as well as retina show marked changes due to injury from x-irradiation. These differences between treated and untreated animals are sufficient to indicate that pretreatment with glutathione is definitely protective for 800 r irradiation and at least moderately protective against the described clinical changes at the higher levels of irradiation.

Irradiation with 2240 and 6000 r resulted in significant decreases in succinic dehydrogenase, cytochrome oxidase, and glucose-6-phosphate dehydrogenase activity for all tissues, when compared with controls. Only the glucose-6-PO_4 dehydrogenase activity of iris and ciliary body appeared not to recover 48 hours after irradiation when glutathione was administered.

Protection against ionizing radiation with glutathione was significant in the retina, lens capsule, and iris for succinic dehydrogenase and cytochrome oxidase activity.

M/Sgt. Harvey F. Kohnitz did the color photography; Airmen Michael Walkins Jr. and Paul L. Sanden gave technical assistance, and Mr. Don Curran irradiated the animals.

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The Resistance of the Tissue of the Iris and the Form of the Iris

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The resistance of an elastic membrane to a pressure acting on its surfaces depends on the primary resistance of the membrane and on its stretching. By stretching the resistance increases and the bulging produced by a pressure is reduced; by relaxation the resistance decreases and the bulging produced by a pressure is increased. A membrane of primarily low resistance is stretched more extensively by a given force than a membrane with primarily high resistance, and its gain of resistance is higher than that of the primarily more resistant membrane. In strong stretching the resistances of the two membranes may be about the same, while they may be greatly different when the membranes are relaxed. If the pressure acting on the membrane is changing too, increasing during stretching and decreasing during relaxation, so that during stretching of the membrane both pressure and resistance increase, while during relaxation of the membrane both decrease, the change in the degree of bulging will depend on the rates of change of resistance and pressure. The bulging of a membrane with primarily low resistance may increase in relaxation by the great loss of resistance of this kind of membrane in relaxation, although the acting pressure decreases; the bulging of a membrane with primarily high resistance may decrease in relaxation, the change of pressure being the same as in the first case. Pressure and resistance can change at different rates in different phases of stretching or relaxation, causing a different effect in one phase than in another. If zones of a membrane subject to pressure on one of its surfaces are of primarily different resistance, in strong stretching the zones of lower resistance may be in about the same plane as the whole membrane, while they may bulge more in relaxation owing to the greater loss of resistance of these zones in relaxation. A small portion of the tissue with lower resistance than its surroundings will not be stretched more than its surroundings and there will be no great gain of resistance. This small part of the membrane will be more protruded when the pressure increases, and less when the pressure decreases.

The resistance of the iris to a pressure acting on its surface increases with pupillary contraction and decreases with pupillary dilation. The extent of this change depends on the anatomical structure of the iris and on the contraction of pupillary sphincter and dilator muscles. The change may be different in different zones of the iris. The pressures acting on the surfaces of the iris are a variable pressure difference due to the physiologic pupillary seclusion, which increases during stretching of the iris and decreases during relaxation, and a rather constant small force acting on the most peripheral zone due to outflow and inflow situated in this region. The iris with normal resistance and subject to normal pressure shows a slight bulging, which increases in pupillary contraction and decreases continuously in pupillary dilation. A ring zone of the iris with primarily subnormal resistance may cause protrusion of this zone, which may flatten in pupillary contraction and bulge in pupillary relaxation. This can be obvious in cases where the resistance of a zone of the iris is reduced by a pathological process. A small circumscribed weak area in the iris behaves differently. Its bulg-

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ing increases with pupillary contraction and decreases with pupillary dilation.

Protrusion of a peripheral ring zone of the iris is seen frequently in eyes with narrow angle and with a tendency toward angle closure. This protrusion increases with pupillary dilation and decreases with pupillary contraction. This behavior suggests that the protrusion may be due to a subnormal resistance of this zone of the iris. The small force due to inflow and outflow acting on the extreme peripheral zone has some effect also. Protrusion of the iris due to increased pressure caused by increased physiologic seclusion with normal, approximately uniform resistance of the iris would be expected to result in a bulging of the whole iris outside the ring of relative obstruction, with more bulging in pupillary contraction and less bulging in pupillary dilation. The supposedly weak zone could comprise only the extreme periphery of the iris or a large ring portion of the iris, causing protrusion of a narrow or of a large peripheral ring zone of the iris, as seen in these cases. The peripheral protrusion may show places of more protrusion separated by less protruded portions, demonstrating obviously the importance of the resistance of the tissue. This peripheral protrusion, its form, and its behavior in pupillary movement strongly suggest that weakness of the peripheral iris may be a primary causative factor in cases of narrow angle and angle closure.

Summary

The effect of changes of resistance of the tissue of the iris and of parts of it on the form of the iris is discussed.

Low resistance of the tissue of the peripheral iris is suggested to be a primary factor in cases of narrow angle and angle closure.

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Anaglyphic Phenomena in Anomalous Correspondence

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It long has been known that when some strabismus patients are wearing anaglyphic glasses, such as a red filter before one eye and a green filter before the other, they observe part of a white screen to appear red and other parts green. It is our purpose to describe anaglyphic phenomena noted by patients with various types of anomalous correspondence. These phenomena can be applied to the diagnosis of this anomaly. Also, their occurrence throws some light on the nature of binocular vision in strabismus.

The anaglyphic phenomena are elicited best when the patient looks at a brightly lighted unmarked white screen while wearing red and green filters. The filters must be so balanced that the light stimulus is of nearly equal intensity to the two eyes. It generally is best to have the patient standing 3 to 4 ft. from the screen; at this distance a screen 1 meter wide is adequate and the patient is able to point out what he sees on the various parts of the screen. The distance may have to be varied to be certain that parts of the screen are visualized by both macular regions.

First, consider the phenomena observed by a person with normal binocular vision. Viewing the screen with anaglyphic glasses, the average normal adult will describe a mixture of the red and green or alternate predominance of red or green. Color rivalry may be complete or patchy, but in no instance does the person see the screen as a bright red or green, as in monocular vision.[1]

The patient with esotropia or exotropia with normal correspondence and good visual acuity describes a similar pattern modified only by the magnitude of his deviation and the degree of his binocular awareness. For example, patients with normal correspondence and a high degree of amblyopia in the deviating eye typically describe the color in the central area of the screen as being the same hue and intensity as if they were viewing it monocularly. Stated otherwise, these patients demonstrate a constant predominance of the fixating eye instead of normal retinal rivalry. Patients with normal correspondence and good visual acuity who have acquired a horizontal deviation will see parts of the screen as double. They see pure colors on either side where the two images of the screen do not overlap. The areas of pure color appear uncrossed in esotropia * and crossed in exotropia, as would be expected with diplopia in normal correspondence. In long-standing untreated anomalous correspondence quite a different pattern is observed. It is quite constant and merits detailed description.

The most typical findings are in patients who have a horizontal deviation with harmonious or nearly harmonious anomalous correspondence. In esotropia, the findings are most striking if the blind spot of the deviating eye overlaps the fixation area and visual acuity is normal in each eye.[2] For example, if such a patient is standing 3 ft. from the screen and is fixating the central area of the screen with his right eye, rays of light from this area strike the macular region of this eye but are imaged on the blind spot and nasal retina of the deviating left eye. The left third of the screen is imaged on the retina just temporal to the macula in the fixating right eye, but in the

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Part of a study being conducted under a grant from the Oregon State Elks Association.

From the Department of Ophthalmology, the University of Oregon Medical School. Orthoptic Technician (Miss Wahlgren).

* This applies only if the screen is farther from the patient than the point of crossing of his visual axes.

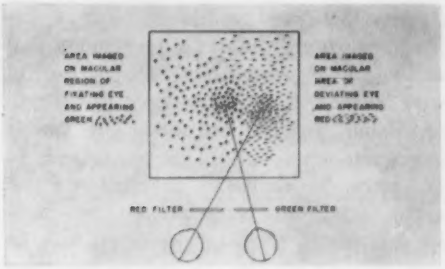

AREA IMAGED ON MACULAR REGION OF FIXATING EYE AND APPEARING GREEN
AREA IMAGED ON MACULAR AREA OF DEVIATING EYE AND APPEARING RED
RED FILTER
GREEN FILTER

Fig. 1.—Left esotropia.

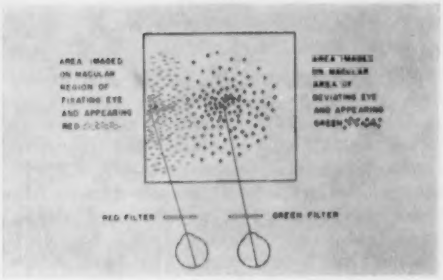


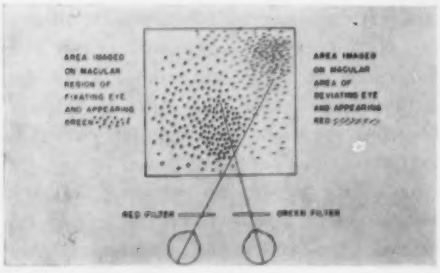
Fig 2.—Left exotropia.

deviating left eye it is imaged on the retina nasal to the optic disc, that is, 10 degrees farther from the fovea than in the right eye. The right one-third of the screen is imaged on the macular region of the deviating left eye but on the retina nasal to the nerve head of the fixating right eye. Now consider what is observed by such a patient wearing a red filter before the fixating right eye and a green filter over the deviating left eye. He describes most of the central area and all the left half of the screen as appearing red. Most of the right side of the screen appears green, but there is no sharp dividing line between the red and green (Fig. 1).

In exotropia with harmonious or slightly subharmonious anomalous correspondence similar division of the screen into fields of red and green is described, except that the colors appear uncrossed. If the red filter is before the right eye and the right eye is fixating the central area, then the right half or two-thirds of the screen is seen as red and the left side as green (Fig. 2).

Three patients were tested who had a harmonious vertical anomalous correspondence in addition to esotropia. In all, the division of colors on the screen corresponded to the vertical deviation as well as to the horizontal. For example, a patient with left esotropia and hypertropia with both horizontal and vertical anomalous correspondence wore a red filter over O. D., which fixated, and a green one over the deviating left eye. He described the central and left inferior part of the screen to be red, while the right superior third of the screen appeared green (Fig. 3). The separation of the hues corresponded to his afterimage test.

Fig. 3.—Left esotropia and left hypertropia.


AREA IMAGED ON MACULAR REGION OF FIXATING EYE AND APPEARING GREEN
AREA IMAGED ON MACULAR AREA OF DEVIATING EYE AND APPEARING RED
RED FILTER
GREEN FILTER

In each of the three circumstances described above, division of the color fields corresponded to the deviation, but not all patients with anomalous correspondence observed this phenomenon.

There are notable exceptions to this observed divided color field phenomenon. For example, patients with a high degree of amblyopia, eccentric fixation, and anomalous correspondence usually describe the whole screen as having the same hue as the filter worn before the fixating eye. Then, some patients who have had a large deviation partially corrected by surgery in the presence of anomalous correspondence may not show the divided color field phenomenon. In some patients with intermittent exotropia and variable correspondence, the phenomenon may be present when the visual axes are divergent and absent when alignment is normal.

We have found no references to this divided color field phenomenon in anomalous correspondence in ophthalmologic literature

in recent years; however, in 1939 Verhoeff [3] wrote the following:

> The third test, employed to show that in cases of strabismus both eyes play an important part in vision, is equally simple. A red transparent screen is placed before the fixing eye, and a green transparent screen, before the other eye. The subject is instructed to maintain fixation on a small object situated at a distance of about 1 meter and usually, therefore, well beyond the crossing point, even if the strabismus is convergent. A white disk, 21 mm. in diameter, on a black background is now placed just above or to one side of the point of fixation. To the subject it appears red. It is then placed on the primary axis of the squinting eye at about the same distance away. Now it appears green. It is then slowly carried across from this position toward the other. When at an intermediate position, while still appearing to be the same object seen with the same eye, it suddenly appears red, without sudden change in its apparent position. Evidently the position at which it appears to change color indicates the line which at the time divides the visual field seen by one eye from that seen by the other.

Then, in 1949 Thaddeus Murroughs,[4] a Chicago optometrist, wrote to one of us (K. C. S.) that he had observed similar color phenomena. He projected alternate red and green bars on a white screen while having some strabismus patients wear red and green goggles. Some of these patients observed green bars alternating with white bars on one side of the screen. They observed red bars alternating with white bars on the other side of the screen. He found a difference between exotropia and esotropia. Later, Murroughs and Shepherd [5] described the use of anaglyphic tests in the optometric literature. Also, in the manual prepared by the Keystone Company for their projection haploscope (stereomotivator), divided color fields are described as evidence of anomalous correspondence. The red and green goggles prepared by this company are particularly suitable to bring out the divided color field phenomenon.

At present it is not possible to fully explain this divided color field perception which occurs in some patients with strabismus. It is additional evidence that even though the object of fixation may be viewed monocularly there is some degree of simultaneous binocular perception in these patients; however, it must not be assumed that under ordinary visual conditions the patient with anomalous correspondence has a field of vision divided into areas of purely monocular perception. This concept can be proven to be erroneous if small red and green targets are projected on the screen. In this instance, the green target can be seen only by the eye covered by the green filter and vice versa. In patients who are observing the divided color fields, both of the projected red and green targets can be visualized on either half of the screen; therefore, the field of binocular vision in anomalous correspondence probably is not made up of fields of monocular perception.

The divided color field phenomenon is best explained as a predominance of the macular region of each eye over peripheral retinal areas in the other eye which have become functionally corresponding in an anomalous manner. This predominance is elicited by presenting different stimuli of equal intensity to these areas. Stated otherwise, in anomalous correspondence, anatomically corresponding areas, such as the two maculas, no longer have a common visual direction. Instead, they may acquire different visual directions in general accordance with the deviation. For example, in a left esotropia of 30 degrees with harmonious anomalous correspondence the macular region of the left eye acquires, in binocular vision, a visual direction as if it were a retinal area nasal to the nerve head of the right eye. The retinal elements nasal to the right nerve head have less "sensitivity" to contour and hue than the macular region of the deviating left eye; therefore, in a left esotropia with harmonious anomalous correspondence one would expect predominance of sensations from the left eye in the visual field to the right of fixation. The converse would be true in left exotropia with anomalous correspondence, that is, the macular region of the deviating left eye would receive images from the left of the fixation point and would predominate over

peripheral retinal areas in the right eye. In vertical anomalous correspondence the division of color field would be expected to be and is along an oblique axis.

The divided color field phenomenon justifies further investigation, but, even at present, it is a simple aid in diagnosis that can be used even with preschool children. Nothing is required but a white background and a pair of balanced red and green glasses. Presence of the phenomenon in a child with a manifest deviation establishes the diagnosis of a harmonious or nearly harmonious stable type of anomalous correspondence. On the other hand, absence of the phenomenon does not rule out anomalous correspondence or establish the presence of normal correspondence.

Summary

Typical phenomena are described by patients with a stable harmonious or nearly harmonious anomalous correspondence as they look at the center of an unmarked white screen while wearing properly balanced anaglyphic (red and green) glasses. If there is good visual acuity in each eye, patients observe part of the screen to be red and part to be green. The separation of the fields is in accordance with the deviation of the visual axes, and the hues appear brightest in the regions of the screen perceived by the two macular regions. In exotropia, the visual axis of the deviating eye is directed to the homolateral side, and so this part of the screen appears the same hue as the filter worn before this eye. The converse is true in esotropia. For example, if a red glass is worn before the right eye the left part of the screen appears red. The phenomenon is best explained on the basis of predominance of the macular region of each eye over the abnormally corresponding peripheral retinal areas in the other eye when dissimilar stimuli of equal intensity are presented to these regions. It does not prove that the field of vision in harmonious anomalous correspondence is divided into fields of monocular perception.

3181 S. W. Sam Jackson Park Rd. (1).

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The Effect of Cell Suspensions upon the Development of Cataracts in Irradiated Mice

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Cysteine, administered parenterally to rats prior to total-body irradiation, has been reported by Patt and his co-workers [1] to increase the survival of the treated animals, whereas sodium chloride given before radiation or cysteine given afterwards does not. Von Sallmann [2] has described a deterrent effect of cysteine administered intravenously to rabbits before a single exposure to 1500 r delivered to the eye. Jacobson and his associates [3] and Lorenz et al.[4] have shown that hemopoietic cell suspensions or tissue transplants given subsequent to x-radiation have a significant effect upon the survival of rats, mice, and rabbits. There have been no reports that such postirradiation treatment might influence the development of cataracts.

It was observed that postirradiation treatment with mouse embryo cells appeared to have a deterrent effect upon the development of cataracts in a single group of mice that had been exposed to 750 r total-body x-radiation as part of a long-term study of radiation injury. The investigation described in this paper was conducted to learn whether the injection of cellular substances after irradiation might modify the development of cataracts.

Materials and Methods

CF No. 1 female mice, weighing 22 gm., were used as the recipient animals. The cells tained from the tissues of CF No. 1 mouse used for postirradiation injection were obembryos or from baby mouse spleen, livers, and bone marrow. The donor mice were killed by cervical fracture. Embryo tissue was obtained by making a median incision in the abdominal cavity of the pregnant mouse, removing the entire embryonic sac and placing it in cold Locke's solution. The livers and spleens were then removed from the embryo, and a homogeneous cell suspension was produced by repeatedly drawing the mixture into a 2 cc. syringe and expelling it. The number of nucleated cells per cubic millimeter was determined by making a dilution with 2% acetic acid in a white-blood-cell-counting pipette and counting the cells in a standard hemocytometer. Cell suspensions were diluted with Locke's solution so that each 0.5 cc. contained the required number of cells. All injections were made a few minutes after the cell suspensions had been prepared and within four hours after irradiation. Cells from the baby mouse tissues and bone marrow were prepared in a similar manner.

Mice were subjected to total-body x-radiation ranging between 750 and 975 r before administration of the cell suspensions. Nonirradiated mice and mice that were spleen-shielded and body-shielded during irradiation served as controls. X-rays were generated by a 250 kvp Maxitron machine operating at 30 ma. A 1.0 mm. Al and a 0.25 mm. Cu filter were used. The half-value layer in copper of the filtered beam was 1.04 mm. The exposure rate averaged 33.8 r per minute at a distance of 79 cm.

At various intervals after irradiation the pupils were dilated with 2% homotropine hydrobromide solution, and the lenses were

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TABLE 1.—*Average Severity of Cataract in Mice Studied Ten to Twelve Months After Irradiation (750 R)*

Cells Injected, No. $\times 10^6$	Treatment	Number in Group	Average Severity of Cataract	Number with Cataracts	Number Without Cataracts
0.3-0.75	Embryo cells	4	1 3/7	1	3
----------	Spleen shielded	6	7 3/5	6	0
1.5-5.0	Bone marrow cells	9	7 1/9	9	0
9.0	Embryo cells	7	7 2/7	7	0
0.75-1.5	2-day liver cells	2	7 1/2	2	0
1.3	Liver cells	3	7 2/3	3	0
2.2	Spleen cells	2	8	2	0
0.07-0.27	Embryo cells	9	3 5/9	6	3
2.5	Bone marrow cells	5	6 3/5	4	1
3.5	Spleen/liver cells	7	8	7	0
0.5	Liver cells	8	7	8	0
----------	None, control	10	0.6	0	10
3.5	Liver cells	5	7 1/5	5	0
0.5	Bone marrow cells	2	4	2	0
0.5-3.5	Spleen cells	9	2 5/9	3	6

examined by means of a Zeiss slit lamp. The treatment to which the animals had been subjected was unknown to the observer. However, the animals were presented in turn from a given cage so that animals receiving the same treatment were presented in groups of 6 to 12, depending upon survival rates.

The severity of cataract was graded according to the scheme of Christenberry et al.[5] Values ranged from 0, for a transparent lens, to 4, for a complete cataract. Thus, bilateral complete lens opacities constituted a severity of 8. The severity of cataract in each treatment group was then averaged.

At the suggestion of Prof. Leonard J. Savage, Chairman of the Department of Statistics, The University of Chicago, animals were divided into two groups: no cataract (a severity of 3 or less) and cataract (a severity of 4 or more). It was believed this would reveal intragroup differences in the event that the cell treatment combined with some unknown (and entirely postulated) physiological or environmental factor to modify the development of radiation-induced cataract.

Results

Table 1 shows the results obtained from the first series of mice, whose lenses were graded at 10 to 12 months following irradiation. A possible deterrent effect of the injection of 0.3 to 0.75×10^6 embryo cells and 0.5 to 3.5×10^6 spleen cells was suggested by both the mean severity of cataract and the division of animals into cataract and noncataract groups.

In the second study, the animals were examined before irradiation to eliminate all with cataract or other ocular anomalies. In addition to the postirradiation administration of cells, the bodies or the spleens of the mice were shielded. The lenses of these animals were studied five months after irradiation, and the results are given in Table 2.

The data indicate that there is a fairly wide range in the rate of development of cataract under the conditions of the experiment. It is evident, however, that the administration of cell suspensions does not modify the development of radiation-induced cataract. A study of the lenses of all mice that had received cell suspensions during the

TABLE 2.—*Average Severity of Cataract in Mice Studied Five Months After Irradiation*

Embryo Liver Cells Injected	Treatment	Number in Group	Average Severity of Cataract	Number with Cataracts	Number Without Cataracts
	Control: body shielded; Locke's solution (800 r)	37	4.13	27	10
	Control: spleen shielded; isotonic saline (975 r)	27	4.61	18	9
2.5×10^6	Body shielded; mouse embryo cells (800 r)	40	4.2	31	9
	Not irradiated	9	0.22	0	9
2.5×10^6	Spleen shielded; mouse embryo cells (975 r)	18	3.55	10	8

TABLE 3.—*Effect of Irradiation on Lenses of Mice* *

Cells Injected, No. $\times 10^6$	Treatment	Number in Group	Average Severity of Cataract	Number with Cataracts	Number Without Cataracts
0.55–10.0	5-wk. bone marrow cells	34	5.5	24	10
0.6 –10.0	12-wk. bone marrow cells	23	6.3	22	1
0.6 –15.0	Embryo liver cells	16	6.0	23	0
2.5	2-day spleen cells	4	5.0	5	0
0.5	Spleen and liver cells	6	6.7	6	0
0.5 – 9.1	Liver cells	6	5.0	6	0
0.5 – 9.7	Embryo liver cells	20	7.2	20	0
0.5 – 9.1	2-day liver cells	7	5.6	6	1
	Control	7	1.6	1	6
	Control (spleen shielded + saline)	24	6.1	23	1
2.5	Embryo liver cells and spleen shielded	30	7.0	29	0
2.5	Bone marrow, liver, or spleen cells 600 r only	22	3.5	17	5
		10	4.2	8	2
0.5	Embryo liver cells	10	4.2	7	3
0.5 – 0.58	2-day liver or spleen cells	8	6.5	8	0

* The amount of radiation administered to these animals varied between 800 and 975 r. The lenses were studied between three and six months after irradiation. These variables account for the intragroup differences in cataract severity.

period of study indicated an absence of protective effect upon the lenses (Table 3).

Comment

The chance observation of the failure of cataracts to develop in mice that had survived a lethal and cataract-inducing exposure to radiation after being treated with cell suspension led to this study. Since it was known that pretreatment with cysteine enhanced survival and minimized the development of cataract, it was postulated that postirradiation injections of cell suspensions, which markedly improve the survival rate, might have a similar effect. However, the lenses were not found to be protected under these circumstances.

Investigation revealed that the animals that failed to develop cataracts were all irradiated upon the same day. Although their survival rates were similar to other irradiated and treated animals, an experimental artifact seemed to be the most likely explanation.

Summary

The postirradiation administration of various cell suspensions that have been found to be effective in prolonging the lives of lethally-irradiated mice does not protect the animals against the development of cataract.

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Effect of X-Rays on Partially Shielded Lens of the Rabbit

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Goldmann and Liechti,[8] Alter and Leinfelder,[1] Puntenney and Shoch,[10] and von Sallmann et al.[12] have shown that irradiation of the axial core of the lens does not lead to any opacity, whereas irradiation of a sector of lens including part of the periphery causes opacities in the area irradiated. These results are clear-cut and leave no doubt that damage to the periphery of the lens is the genesis of radiation opacities. A puzzling feature, however, has been that irradiation of a sector, or even of half the lens, does not produce complete opacity within the area irradiated but simply small cortical opacities, which presumably represent the immediately damaged epithelial cells and their progeny. For example, Puntenney and Shoch,[10] using a dose of 4000 rad, found that irradiation of the whole eye of the rabbit produced mature cataract, in three to five months, but that irradiation of one-half of the lens produced only vacuolar cortical opacities in the area irradiated. This result was confirmed by Leinfelder and Riley,[6] who first commented on the absence of complete opacity formation in the area irradiated, even after heavy doses. They found that even when 12,000 rad was given to two lens quadrants, an absorption of twice the energy needed to cause a complete cataract when an entire lens was exposed, complete opacification of the exposed quadrants was not observed.

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We have repeated experiments of this kind and confirm that irradiation of the axial core of the lens of the rabbit with a 5 mm. diameter beam of 1600 rad causes no visible damage, whereas irradiation of an equal peripheral area with the same dose causes cortical opacity in that area (Fig. 1). This does not develop to a complete opacity even within the area irradiated over a period of two years (Pirie[7]). The question therefore arises of what is the minimal area of the lens that must be irradiated to produce a complete opacity, in which not only do the epithelial cells that are immediately damaged by radiation become optically abnormal but the inner fibers of the lens also degenerate and become opaque. We have therefore irradiated the lens in such a way that either the beam of x-rays passes through the total periphery while the axial core is shielded with a 5 mm. diameter lead stop (the exact reverse of our previous experiment) or, using the same lead stop placed eccentrically, the axial core of the lens plus about three-quarters of the total periphery is irradiated (Fig. 2). The total area of the lens irradiated is the same in the two cases, as the same lead stop is used, but in one case the total periphery is irradiated and in the other case only three-quarters of it. An advantage of using x-ray beams matched for area and dose in this way is that any differences observed between animals irradiated in these ways cannot be attributed to difference in area of the beam cross-sections leading to differences in the total energy absorbed in the eye. The results show that damage to more than three-quarters of the periphery of the lens of the rabbit is necessary for complete cataract.

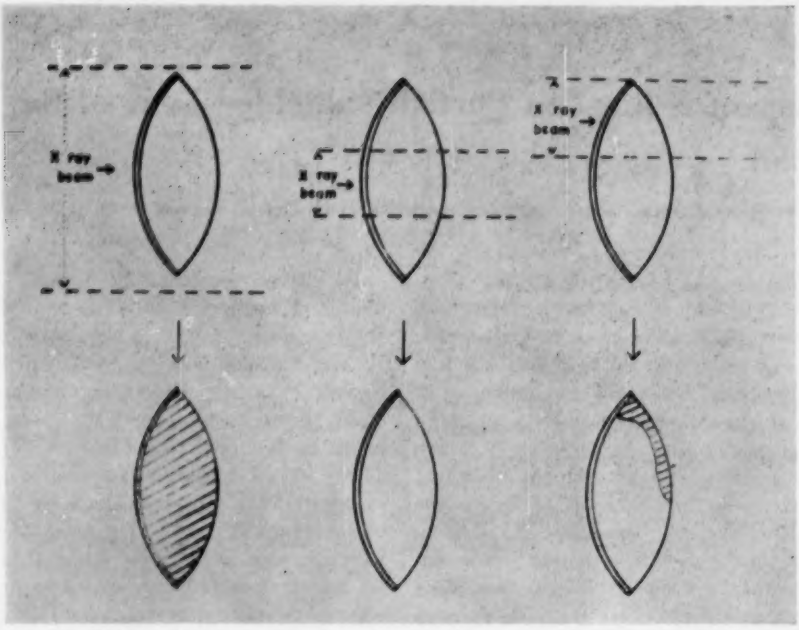

Fig. 1.—Effect of irradiating the whole, the axial core, or part of the periphery of the lens.

These results have been briefly reported previously (Pirie [5]).

Damage to the lens was assessed clinically and also by comparison of glutathione in the irradiated lens with that of the normal fellow lens. We have found that loss of glutathione is an early biochemical change after radiation and that it is progressive during opacity development (van Heyningen, Pirie, and Boag [5]). Difference in weight between the irradiated lens and its fellow was also determined, as there is a slowing of lens growth after irradiation (van Heyningen, Pirie, and Boag [5]), with a terminal swelling and weight increase.

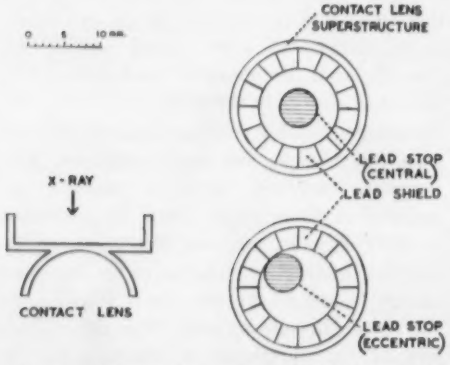

Fig. 2.—Contact lens and lead shields used in Experiment 2.

Methods

Animals.—Dutch rabbits from 6 weeks to 6 months old were used.

Irradiation.—The x-rays were generated at 200 kv. and filtered by 0.5 mm. Cu and 1 mm. Al. The doses used ranged from 1600 to 2000 rad. The rabbits were anesthetised with pentobarbital (Nembutal), and, after insertion of the contact lens and lead shields into the right eye, were placed so that the contact lens superstructure was apposed to the orifice of the lead tube through which the x-ray beam was passed. Movement of the eye during irradiation was thus reduced as far as possible.

Experiment 1. Irradiation of Axial Core or of Small Area of Periphery.—A contact lens having a superstructure as in Figure 2 was inserted into the right eye. Lead shields

4 mm. thick were placed on the contact lens. These shields were 16 mm. in diameter and had either a central aperture 5 mm. in diameter or an eccentric aperture 5 mm. in diameter. The eccentricity was such that the center of the aperture was 3.2 mm. or 4.3 mm. from the center of the lead shield. With these eccentric apertures an area of the periphery of the lens is irradiated.

Experiment 2. Irradiation of Total Periphery with Center Shielded or Irradiation of About Three-Quarters of Periphery and Center.—The contact lens was inserted into the right eye as before and a 6 mm. wide ring of lead was then placed within the contact lens superstructure. The inner diameter of this ring shield was 11 mm., which is a little larger than the diameter of the lens. Within this ring a 5 mm. diameter lead plug was fixed with adhesive tape so that it was either central in the ring or peripheral (Fig. 2).

Clinical Examination.—The rabbits were examined with slit lamp and ophthalmoscope, at first at weekly intervals and later at monthly intervals.

Extraction and Weight of Lens.—At the end of the experiment the rabbit was killed by an overdose of pentobarbital; the eyes were removed, and the lenses were extracted anteriorly and immediately weighed.

Estimation of Glutathione.—Glutathione was determined by the method of Grunert and Phillips,[4] with extracts of lens prepared as described earlier (van Heyningen, Pirie, and Boag[5]).

Results and Comment

Experiment 1.—Figure 1 and Table 1 show that no opacity at all was produced when the axial core of the lens was irradiated with 1600 rad, whereas we have found, in a large number of rabbits of the same breed and age as those used in this experiment, that 1400 rad given to the whole eye causes the development of complete cataract in 5 to 10 months. A dose of 1600 rad to an area of periphery produced cortical opacities within that area.

The lenses which had been irradiated centrally or peripherally were examined to see if there was any difference in weight or glutathione (GSH) content between them and their normal fellows. In only one lens was there a possibly significant difference in weight after a peripheral irradiation. The total GSH showed slight decrease in two lenses; in one case there was a similar increase. Such changes are not significant.

In those lenses that were irradiated centrally it was possible to estimate the GSH of the axial core by cutting it out of the lens with a trephine 6 mm. in diameter. We found that there was no difference between the irradiated lens and its normal fellow, showing that an area of lens that remains clinically normal after irradiation also retains its GSH. Unfortunately it was not possible to estimate the GSH in the peripheral irradiated sector, as, after extraction of the lens, it was impossible to see the fine cortical opacities and so locate the exact site of radiation.

Experiment 2.—Irradiation of the lens with the 5 mm. lead stop placed centrally (Fig. 2), so that the whole periphery of the

TABLE 1.—*Effect of Central or Peripheral Irradiation* on the Lens of the Rabbit*

Rabbit No.	Position of Beam	Opacity	Duration of Experiment, Yr.	Per Cent Change in Irradiated Lens	
				Weight	GSH
78	Central	None	2	+3	−4
79	Central	None	1.75	----	----
80	Central	None	1.75	0	0
81	Central	None	1.75	0	0
82	Central	None	1.0	0	0
83	Peripheral	Cortical	1.0	−3.5	−6
84	Peripheral	Cortical	1.5	−2.1	0
85	Peripheral	Cortical	1.0	−5.9	+7

* Dose to right eye, 1600 rad. A dose of 1400 rad to the eye is our standard procedure for producing a completely opaque lens in 6 to 10 months.

TABLE 2.—*Irradiation of Total Periphery or of About Three-Quarters of Periphery and Center of Lens*

Rabbit No.*	Dose, RAd	Duration of Experiment, Mo.	Area Irradiated	Opacity	Per Cent Change in Irradiated Lens	
					Weight	GSH
86	1,600	4.5	Total periphery	Complete cataract	+8.5	−68
87	1,560	5	Total periphery	Complete cataract	+4.0	−76
88	2,000	4.5	Total periphery	Complete cataract	+22.0	−90
89	2,000	7.0	Total periphery	Widespread cortical opacities	−24	−47
90	2,000	7.0	Total periphery	Widespread cortical opacities	−19	−33.5
91	1,600	7.0	Three-quarters of periphery & center	Cortical opacities	−17	−30
92	1,600	7.0	Three-quarters of periphery & center	Cortical opacities	−17	−33
93	1,600	7.0	Three-quarters of periphery & center	Cortical opacities	−14	−27
94	2,000	7.0	Three-quarters of periphery & center	Cortical opacities	−15	....
95	2,000	7.0	Three-quarters of periphery & center	Widespread cortical opacities	−23	−43

* Age of rabbits 6 to 7 weeks at time of irradiation.

lens is irradiated, has given complete cataract in three out of five rabbits, whereas irradiation with the stop placed eccentrically, so that a sector of peripheral epithelium escapes, has not given any complete cataracts in five rabbits which were litter mates to those irradiated with the stop in the central position. Table 2 records the clinical and biochemical results.

The complete cataracts developed within three months of the time of radiation, and when the rabbits were killed, one and a half to two months later, the lenses were intumescent and weighed considerably more than the normal fellow lenses. The other irradiated lenses were all lighter than their normal fellows, which we interpret as a slowing of growth after irradiation. Table 2 shows that the clinical and biochemical changes were less marked in those lenses where some periphery was spared than in those in which the total periphery was irradiated, except in one case, Rabbit 95, where the changes were as severe as in Rabbits 89 and 90, the two least affected rabbits of the group in which the total periphery was irradiated. The variability of results is probably due to the difficulty of positioning the contact lens and the eye in the x-ray beam.

The definite result of the experiment appears to be that a complete cataract develops only if more than three-quarters of the periphery of the lens is irradiated. Von Sallmann et al.[12] have reported that, in two rabbits, complete cataract resulted from irradiation with a ring-shaped beam 2 to 3 mm. wide (at the level of the lens) designed to hit the extreme periphery of the lens. The dose was 2100 rep of deuterons (heavy hydrogen nuclei). On the other hand, Puntenney and Shoch[10] found that a ring-

TABLE 3.—*Effect of Radiation of Different Areas of Lens*

Reference	Radiation	Dose	Type of Beam	Result
Goldmann & Leichtl[9]	X-ray	1,500–2,000 rad	Central beam, 4 mm. diam.	No damage
			Peripheral beam, 4 mm. diam.	Vacuolar damage
Puntenney & Shoch[10]	X-ray	4,000 rad	Central beam, 5–6.5 mm. dia m.	2/13* posterior vacuole
			Peripheral ring beam, 1 mm. diam.	
			(a) 4 mm. from center	6/6 peripheral vacuoles
			(b) 5 mm. from center	1/6 peripheral vacuoles
			Semicircular aperture	5/6 vacuolar opacities
			No shield	18/20 complete cataract
Leinfelder & Riley[8]	X-ray	1,000–11,800 rad	One quadrant of lens irradiated Two quadrants of lens irradiated	No complete cataracts; only vacuolar cortical changes observed
von Sallmann et al.[12]	Deuterons	2,100 rep	Central beam, 3–5 mm. diam.	1/1 no cataract or visible damage
			Peripheral ring beam, 2–3 mm. diam. at lens	2/2 complete cataract
Pirie & Flanders (this paper)	X-ray	1,400 rad	Central beam, 5 mm. diam.	5/5 no visible damage
			Peripheral beam, 5 mm. diam.	3/3 cortical opacities in irradiated area
	X-ray	1,600–2,000 rad	Central stop, 5 mm. diam.	3/5 complete cataract
			Peripheral stop, 5 mm. diam.	6/6 cortical opacities

* Number of rabbits affected/total number in group.

shaped beam 1.0 mm. wide directed to the extreme lens periphery caused only vacuolar opacities when the dose was 4000 rad of x-rays. The beam used in our own experiments is 3.0 mm. wide, and the dose was 1600 to 2000 rad of x-rays. It therefore seems that area of lens irradiated rather than dose is the more important factor, but too much should not be made of this, as age and breed of rabbit may have been different in the different experiments reported. A summary of the results of the present experiment and those referred to is given in Table 3.

The experiments all demonstrate that the lens fibers are dependent on the peripheral tissue (? germinal epithelium) of the lens and that if a small fraction of this remains healthy the fibers will remain normal. This seems to show that fibers lying under damaged peripheral epithelium must be able to get nourishment from contiguous healthy fibers and epithelium. Those radiation cataracts in which total opacity of the lens develops may therefore be considered to have two stages. Radiation damages only the peripheral epithelial cells and perhaps the most newly formed fibers; no damage appears in the axial area of epithelial cells or the main mass of lens fibers. Secondary to damage of the lens periphery and consequent upon this there is loss of transparency of the fibers of the lens. This supervenes only if sufficient periphery has been damaged. Whether other forms of cataract follow this course is unknown. The radiosensitive periphery of the lens contains those epithelial cells capable of division and the most newly formed lens fibers. Histological studies (Poppe [9]; von Sallmann [11]) have shown that radiation damages the nuclei of the germinative epithelial cells, and it is surely of great physiological interest that all or nearly all must be damaged before complete cataract develops. The converse is also of interest, that such a small proportion of epithelial cells can exert so great an influence in maintaining a healthy lens.

We have noticed that, in those lenses which do not become completely opaque, the opacities, which originally lie immediately beneath the capsule, become, as time goes on, overlaid by clear lens fibers. This seems to imply either that the epithelium of the irradiated area recovers and divides to form new normal fibers or that there is spread of healthy epithelium from a contiguous nonirradiated part of the lens.*

Devik [2] has reported that the roentgen reaction in the skin of mice can be modified very markedly by shielding minute areas from irradiation. Devik suggests that migration of nonirradiated epithelial cells in the skin would seem to afford a plausible explanation of the effects, but increased mitosis of shielded epithelial cells was not observed, and he is more inclined to the view that partial recovery of the irradiated cells has taken place owing to the proximity of normal cells. This indicates that normal cells of skin contain some factor(s) of importance to the recovery of epithelial cells that have been injured by x-rays. The same arguments may hold in the lens, which is an epithelial tissue.

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* The question of repair in the irradiated lens is also discussed by Richards, R. D.; Riley, E. F., and Leinfelder, P. J. (*Am. J. Ophth.* 42:[No. 4 Pt. 2] 44, 1956). This paper appeared after our own paper had been submitted.

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Angioid Streaks and Generalized Arterial Disease

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Although histopathologic studies have shown that angioid streaks of the retina and pseudoxanthoma elasticum are only part of a generalized elastic tissue degeneration, which includes the arterial tree, the clinical relationship to arterial disease is less well known. This paper adds 10 patients to those previously reported in the literature, all of whom showed clinical evidence of arterial disease, especially marked in the lower extremities.

Symptoms suggestive of vascular disease may be absent or extreme, depending upon the location of the vessel and the severity of the involvement. When the arteries of the extremities are affected, the patient may notice paresthesias, numbness, chilling, or intermittent claudication. Objective signs may be obvious or detectable only by careful examination. Pulses may be weak or absent. Pulse waves recorded on an oscillometer are ofter reduced or even absent. Vasodilatation tests may demonstrate reduced blood flow. Roentgen examination of the extremities often shows calcification of the major arteries. Vascular involvement other than of the extremities, if of sufficient severity, results in symptoms, depending upon the affected vessels.

Angioid streaks were first described by Doyne [1] in 1889. Their occurrence with pseudoxanthoma elasticum, a disease known to be due to degeneration of elastic fibers, was noted by Grönblad [2] in 1929. Verhoeff [4] (1928), Rowland [5] (1933), and Terry [6] (1934) reported the occurrence of angioid streaks with Paget's disease (osteitis deformans). Grönblad [2] (1929) first suggested that angioid streaks of the retina and pesudoxanthoma elasticum probably occurred on the basis of a systemic degenerative disease involving elastic tissue. Kofler [7] (1917), although with no histologic support, advanced the theory that the streaks were due to ruptures of Bruch's membrane. The cutaneous changes of pesudoxanthoma elasticum have long been known to be due to degeneration of elastic tissue fibers.

Detailed general and ocular pathologic studies were reported during 1938 and 1939 which firmly established angioid streaks and pseudoxanthoma elasticum as occurring on the basis of a generalized elastic tissue degeneration in which the blood vessels frequently participated. Böck [8] (1938) reported the ocular pathological findings from autopsy material from a patient whose general pathological findings were reported by Urback [9] (1938), and Hagedoorn [10] (1939) studied the eyes of another patient whose general autopsy findings were reported by Prick [11] (1938). Both observers demonstrated for the first time that angioid streaks were due to ruptures of Bruch's membrane of the choroid which had occurred on the basis of degeneration of the elastic fibers in the elastic lamina. They also found basophilic staining of this layer associated with granular degeneration. Subsequent studies by Klien [12] (1947) and Verhoff [13] (1948) confirmed their observations.

Urbach [9] (1938), in his general study of autopsy material from a man 44 years of age, reported degeneration of the elastic tissue fibers in the media of the aorta, the brachial arteries, and some of the vessels of the brain. Prick [11] (1938) found degenera-

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tion of the elastic tissue of the coronary arteries, some of the mesenteric arteries, and the renal arteries. Those of the extremities were not studied. Kat and Prick [14] (1940) also reported the histologic studies on the vessels of a thyroid gland removed from a patient with pseudoxanthoma elasticum. The larger vessels of the thyroid gland showed degeneration of elastic tissue fibers of the wall. This histologic evidence seems to firmly establish angioid streaks of the retina and pseudoxanthoma elasticum as part of a systemic degenerative disease of the elastic tissue of the body in which the arterial system participates.

Recognition of the clinical picture of arterial disease associated with angioid streaks and pseudoxanthoma elasticum was probably stimulated as a result of these pathological studies. Although casual mention of isolated signs of vascular disease can be found in the older literature, carefully done studies did not appear until the paper of Ehlers and Marthinsen [15] (1934). Plange [16] (1891) reported a patient with angioid streaks and noted that the patient had a low radial pulse with a flattening of the pulse curve which he interpreted as being due to loss of elasticity. De Schweinitz [17] (1896) mentioned the high incidence of systemic vascular disease in patients with angioid streaks. Holloway [18] (1927) also mentioned this relationship. Scholz [19] (1941) reported a patient whose pulses were absent in the lower extremities. Occasional mention was made in the older literature of cardiac symptoms associated with angioid streaks.

Ehlers and Marthinsen [15] (1934) first reported clinical vascular studies carefully done on a 48-year-old man. This patient had angioid streaks and pesudoxanthoma elasticum. The radial pulses were weak. Oscillometric studies showed a plateau-like pulse tracing. Grönblad and Carlborg [20] (1940) reported the first systematic group study when they reported six patients with peripheral vascular disease. Carlborg [21] (1944) published a monograph which contained an excellent review of the literature and reported studies on 15 patients who showed angioid streaks and peripheral vascular disease. The characteristic findings were weak or absent pulses, diminished pulsations recorded on an oscillometer, and calcification of the vessels of the extremities on roentgen examination.

Scheie and Freeman [22] (1946), while stationed in India with the United States Army and unaware of the previously reported work in the Swedish literature, reported studies done on three soldiers. All of the patients had pseudoxanthoma elasticum and angioid streaks of the retina. Two also showed clinical evidence of occlusive peripheral arterial disease of the extremities. The pulses in the extremities were diminished or absent. Oscillometric tracings showed marked diminution in the pulse wave, and roentgen examination demonstrated calcification of the arteries. The third patient had unexplained hypertension. A biopsy specimen of an ulnar artery was obtained from one of the patients. This vessel was clinically completely occluded. Histologic study demonstrated elastic tissue degeneration with compensatory hypertrophy of the smooth muscle which was thought to have caused obliteration of the lumen of the artery. This was the first pathological study of an artery in which the disease had been diagnosed clinically.

Guenther [23] (1946) reported studies on nine patients in whom he found abnormalities of pulse waves from the peripheral arteries. Dixon [24] (1951) reported a patient with an aneurysm of the intracranial portion of the internal carotid artery. France [25] (1948) reported a patient showing both ocular and skin changes. The blood pressure was lower in the right arm than in the left. The skin of the right leg was cool as compared to the left. Oscillations were lowered to one-half in the right leg. Voison and Lombard [26] (1954) likewise reported, in a 62-year-old woman, disturbances in the circulation of the lower extremities, with decreased oscillometric index of the inferior third of the leg. Kaplan and Hartman [27]

(1954) reported a patient who suffered from gastrointestinal hemorrhage associated with Grönblad-Strandberg's syndrome.

The present paper reports the findings on 10 patients with angioid streaks and pseudoxanthoma elasticum. Special effort is directed towards a survey of the arterial system for any evidence of vascular disease.

Report of Cases

CASE 1.—A 23-year-old white man was admitted to the hospital on March 18, 1946, because of blurring of vision in his left eye of six months' duration. His general health was good. There were no symptoms of systemic disease. His visual acuity was O.D. 6/6, O.S. 6/60.

Ocular Findings.—External examination was negative. Ophthalmoscopic examination revealed typical angioid streaks radiating from a ring around the disc in each eye. In addition, a hemorrhagic macular degeneration was present in the left eye, accompanied by considerable edema. Slit lamp examination: No abnormal changes were found. Examination of visual fields revealed a dense central scotoma in the left eye.

General Physical Findings.—Physical examination was negative except for early changes of pseudoxanthoma elasticum involving the skin on each side of the neck.

Peripheral Vascular Findings.—The radial, ulnar, dorsalis pedis, and posterior tibial pulses were all palpable. Oscillometric readings were normal in the right lower leg but slightly diminished in the left. A vascular tone test disclosed a high grade of vascular tone. An ECG indicated myocardial damage.

Laboratory Findings.—Routine laboratory studies including BUN, blood sugar, serum calcium, and serum phosphorus determinations; a complete blood cell count, and urinalysis were all negative. Serum cholesterol and phosphatase, acid and alkaline, were normal. X-rays of the chest and skull were negative.

CASE 2.—A 22-year-old white man was seen on Aug. 9, 1946, because of sudden loss of vision in the left eye. A history was elicited of some pain in his legs on walking.

Ocular Findings.—Vision was 6/5 O. D. and 6/30 O. S. This could not be improved by glasses. Visual fields revealed a central scotoma O. S. Ophthalmoscopic examination of the right eye revealed the optic nerve to be healthy. The retina had a diffuse mottled appearance. A grayish ring encircled the disc and was irregular, serrated, and about ¼ disc diameter in size. Streaks, which were similar, radiated out from the ring about 3 to 4 disc diameters in length. The left eye was almost identical to the right except for a hemorrhage in the macula.

General Physical Findings.—The skin of the neck showed a brownish discoloration and roughening which had been noted first at the age of 5 years. Lack of elasticity of the skin had become apparent at 18 years of age. The findings were characteristic of pesudoxanthoma elasticum. They were also present in the neck.

Peripheral Vascular Examination.—The right posterior tibial and dorsalis pedis pulses were weak. The left posterior tibial pulse was not palpable. The oscillometric tracings were normal at the wrists but were diminished at the ankles. Roentgen study revealed calcification of the arteries in the thighs. An electrocardiogram was normal.

Laboratory Findings.—Serum calcium, phosphorus, and alkaline and acid phosphatase; blood urea nitrogen; fasting blood sugar; hemoglobin, and complete blood cell count were all normal. The serologic tests were negative and the urine was normal. Chest x-ray was normal.

CASE 3.—A 26-year-old white man was admitted to the hospital on Sept. 2, 1946, because of sudden loss of vision in the right eye. A history of pain in his right leg after walking or running, which increased in severity with further exercise, was elicited.

Ocular Findings.—The visual acuity was O. D. 20/100, O. S. 20/20. This could not be

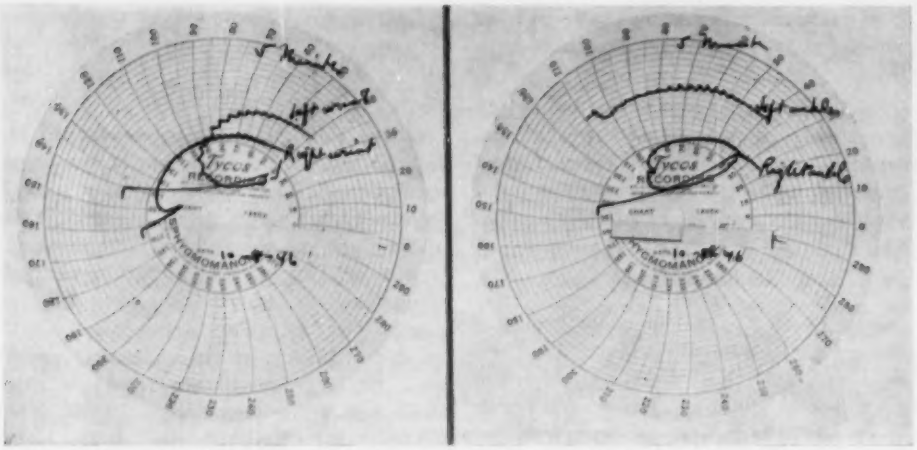


Fig. 1.—Oscillometric tracings showing reduction in amplitude at wrists and ankles.

improved. External examination was negative. Ophthalmoscopic examination of the right eye revealed the media to be clear and the disc normal. A subretinal hemorrhage was seen adjacent to the disc temporally, and it extended into the macula. Many areas of pigmentary disturbances were visible in the macular region. Radiating from the disc were classical brownish angioid streaks. Angioid streaks were present in the left eye but without macular changes.

General Physical Findings.—Inspection of the skin revealed the classical appearance of pseudoxanthoma elasticum over the posterolateral aspect of the neck. Other physical findings were negative except for peripheral circulation.

Fig. 2.—Roentgen study showing calcification in the femoral arteries.

Peripheral Vascular Findings.—The hands and feet felt cool. The radial and ulnar pulses were reduced, and no pulsations were palpable at the ankles. Oscillometric studies showed some reduction at the wrists, great reduction at the left ankle, and complete absence at the right ankle, even during vasodilatation (Fig. 1). Vascular tone test disclosed high vascular tone. The blood flow to the feet was deemed inadequate for proper nutrition of tissues. Roentgen examination of the extremities showed minimal calcification of the femoral artery in the region of the abductor canal (Fig. 2).

Laboratory Findings.—Serum calcium, phophorus, and cholesterol; blood sugar, blood urea nitrogen, and blood chlorides were normal. The hemoglobin, white cell count, and urinalysis were normal.

CASE 4.—A 56-year-old white woman was admitted to the neurosurgical service on May 31, 1949, because of severe pain in the right side of her face and head. In 1933, following spinal anesthesia, she suddenly developed a ptosis of the right upper lid, with severe right supraorbital pain and numbness on the left side of her body,

Fig. 3.—Roentgen study showing aneurysm of right internal carotid artery in the parasellar region.

nuchal rigidity, and diplopia. This gradually subsided, but she did have four or five subsequent less severe episodes of a similar nature. On May 15, 1949, she had sudden onset of pain in the right eye followed by ptosis. On May 20, 1949, she had a precipitous onset of severe, sharp, throbbing right hemicephalgia and later numbness of the right forehead.

Ocular Findings.—Visual acuity was 6/6 in each eye. Each fundus showed typical angioid streaks. A bruit could be heard over each eye, less pronounced over the left. There was right lateral rectus palsy and a nearly complete right ptosis. The pupil on the left was slightly miotic. There was anesthesia of the first division of the right fifth cranial nerve, with diminished right corneal reflex and hypesthesia of the remaining branches of the fifth nerve.

General Physical Findings.—General physical examination was negative except for peripheral vascular studies.

Peripheral Vascular Findings.—The pulses at the wrists and lower legs were very weak. The oscillometer tracings were very reduced at wrists and ankles and were only slight improved by vasodilatation. X-rays of the extremities at this time showed vascular calcification in the left upper arm and the right lower leg.

Laboratory Findings.—No significant abnormality was found. An x-ray of the skull showed erosion of the dorsum sellae on the right, asymmetry of the orbital fissure on the right due to erosion, and a 2 mm. shift of the pineal to the left. A cerebroangiogram on June 2 showed evidence of an aneurysm of the right internal carotid artery in the parasellar region (Fig. 3). Calcification also was present in the wall of the aneurysm.

CASE 5.—A 45-year-old white woman was first seen on June 25, 1948, and again in July, 1952. Her chief complaint at the time of her initial visit was recent loss of vision in her left eye. Her general health was good. There were no symptoms referable to her circulation.

Ocular Findings: Her visual acuity was O. D. 6/6−4, O. S. CF at 2 ft. (60 cm.). This could not be improved by correction. Her eyes were normal except for fundus changes. The media were clear. The discs were healthy. They were surrounded by a reddish-brown irregular ring of the type seen with angioid streaks of the retina. Typical streaks radiated to just beyond the midperiphery of the fundus. The right macula was healthy. The left fundus was similar except for pigmentary degeneration of the macula with hemorrhagic macular degeneration.

Fig. 4.—Photographs showing typical cutaneous changes in the skin. *A*, about the mouth; *B*, side of the neck; *C*, axilla.

General Physical Findings.—Dermatologic changes characteristic of pseudoxanthoma elasticum were seen about her mouth, laterally on her neck, and in the axillary regions, where typical folds had occurred (Fig. 4).

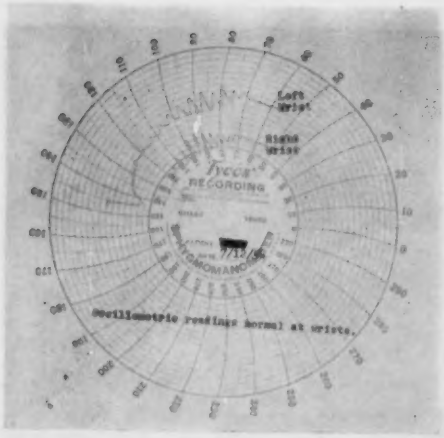
Peripheral Vascular Studies.—The left radial pulse was weaker than normal, but the ulnar pulse was normal. The right radial pulse was palpable, but the ulnar pulse was absent. The dorsalis pedis pulses were weak, and the posterior tibial, as well as the popliteal, pulses were not palpable. Oscillometric examination revealed greatly reduced oscillations in the legs even as high as the thighs (Fig. 5). The oscillations were smaller at the right wrist than at the left, although diminished in each (Fig. 5). Color changes in the skin of the feet on elevating the legs and in the dependent position were suggestive of ischemia in both feet, although they were warm and equal in temperature. The vascular consultant's opinion was that there was extensive arterial occlusive disease. Roentgen examination of the extremities showed calcification of the left femoral and posterior tibial arteries through their course. An ECG was normal.

Laboratory Findings.—Routine studies were negative, including determinations of serum calcium and phosphorus, blood urea nitrogen, and fasting blood sugar and a complete blood cell count and urinalysis.

CASE 6.—A 44-year-old white woman was admitted to the neurological service in July, 1951, because of blurring of vision of about two years' duration. She also complained of "weak legs."

Ocular Findings.—Visual acuity was O. D. 6/9, O. S. 6/6, without correction. The right pupil was slightly larger than the left, but both reacted normally. A paralysis of the left external rectus muscle was present. The disc margins were blurred. Papilledema of 2 D. was present bilaterally. Typical angioid streaks encircled each disc and extended out onto the retina. Visual fields showed enlarged blind spots. The maculae were normal.

General Physical Findings.—The blood pressure was normal. Typical changes of pseudoxanthoma elasticum were found in



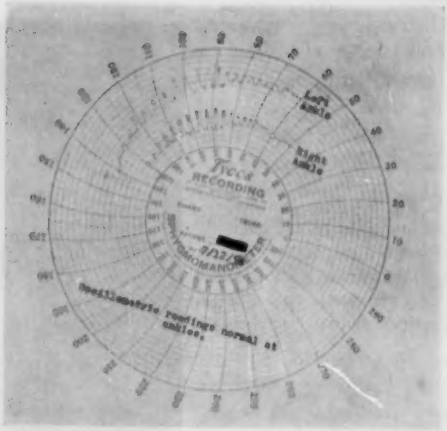
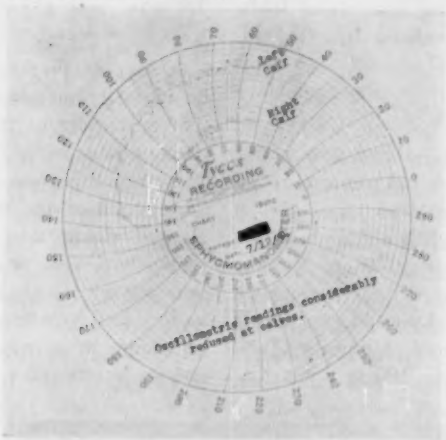
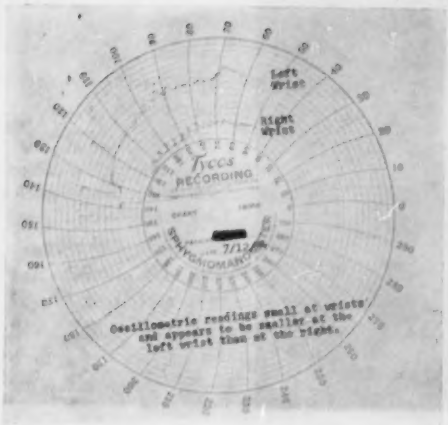
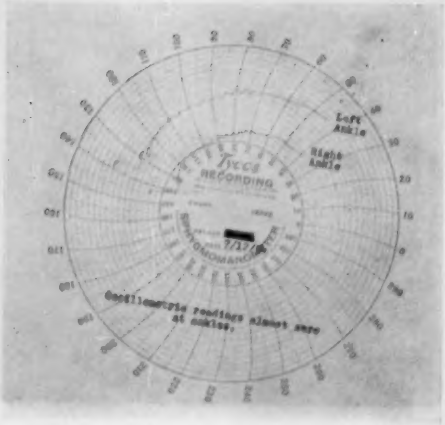


Fig. 5.—Above, normal oscillometric tracings taken at wrists and ankles. Below, oscillometric readings showing marked diminution in pulsations at calves, wrists, and ankles.




Left Wrist
Right Wrist
TYCOS RECORDING
Oscillometric readings small at wrists and appears to be smaller at the left wrist than at the right.



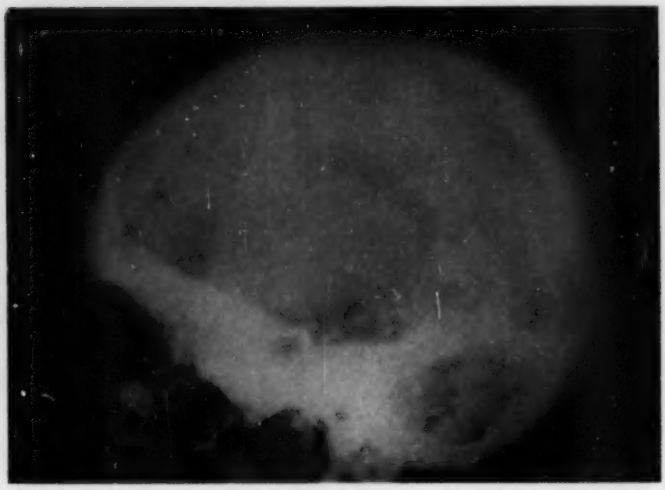


Fig. 6.—Roentgen study showing increased density of bone at the base of the skull, with areas of increased and decreased density elsewhere.

the neck and axillae and antecubital folds. The patient had generalized lymphadenopathy. Bilateral external carotid aneurysms were detectable. The liver was palpable 3 fingerbreadths below the costal margin.

Laboratory Findings.—Blood urea nitrogen, fasting blood sugar, and complete blood cell count were normal. The blood carbon dioxide content was slightly elevated. Serum calcium was 10.5 mg. per 100 cc., and the serum phosphorus was definitely elevated, 7.5 mg. per 100 cc. Acid phosphatase was 0, and the alkaline phosphate, 4.0, units. Total protein was 7.1 gm. per 100 cc.; albumin, 3.3 gm., and globulin, 3.8 gm. Serologic tests were negative.

X-rays of the skull revealed the base to be markedly thickened and sclerotic (Fig. 6). The remainder of the skull showed various areas of increased and decreased density. Marked calcification of the falx was present. The bones of the thoracic cage and spine showed demineralization suggestive of a metabolic disease or osteitis deformans. The bone survey reported generalized demineralization and hypertrophy, with obvious calcification in a number of vessels. The entire picture was thought to be due to

Fig. 7.—Roentgen study demonstrating calcification in the renal arteries and celiac axis.

hyperparathyroidism. Paget's disease (osteitis deformans) could not be excluded.

Peripheral Vascular Findings.—The ulnar, posterior tibial, dorsalis pedis, and popliteal pulses were absent. Oscillometric tracings demonstrated markedly reduced pulses at the wrist and ankles with absent oscillations at the knees. Roentgen study revealed calcification of the arteries in the thighs, the posterior tibial arteries, the coeliac axis, and the right and left renal arteries and bilateral calcified common carotid aneurysms (Fig. 7).

CASE 7.—A 63-year-old white man was admitted in September, 1951, because of gradual visual loss in the left eye of five years' duration. Four months prior to admission the vision in the right eye had suddenly become even worse. He stated that he had been treated previously for a gastric ulcer. He also had noticed pain in the calf of his right leg after walking about half a block.

Ocular Findings.—Visual acuity: O. D. 6/150, O. S. 6/22, with correction. The eyes were normal except for ophthalmoscopic findings. The optic nerves were healthy. Minimal changes of hypertensive retinal arteriolarsclerosis were seen in the retinal arterioles. Each disc was surrounded by a grayish-brown ring separated from the disc from which radiated several grayish-brown streaks typical of angioid streaks of the retina. Bilateral macular degeneration of the Junius Kunt type was present. Visual fields demonstrated central scotomas bilaterally.

General Physical Findings.—General physical examination was negative except for early dermatologic changes of pseudoxanthoma elasticum. X-rays of the skull, chest, and long bones were negative.

Laboratory Findings.—Results of laboratory tests, including determination of serum calcium, were normal.

Peripheral Vascular Findings.—The dorsalis pedis pulses were absent. The posterior tibial pulse was absent on the right and diminished on the left. The popliteal pulse was absent on the right and diminished on the left. The radial pulse was normal. Oscillometric studies showed a diminished amplitude at both wrists, thighs, and ankles. A vasodilatation test indicated reduced capacity for blood flow through the feet. X-rays of the extremities demonstrated marked calcification of the iliac, femoral, dorsalis pedis, and post-tibial arteries of the right leg (Fig. 8). It was less marked on the left. An ECG was within normal limits.

CASE 8.—A 55-year-old white woman was first seen on Oct. 21, 1952, because of rather sudden visual loss in the left eye which had been preceded by rather profound loss of vision in the right eye three years previously. On questioning she stated that she also had noticed a cramp-like pain in the left foot after walking a short distance.

Ocular Findings: Visual acuity: O. D. CF, O. S. 6/22, without correction; O. D. CF, O. S. 6/12, with correction. The findings were negative except for ophthalmoscopic examination. The media was clear; each disc was healthy. Unusually red angioid streaks were present, surrounding the disc and radiating under the retina to the midperiphery. Bilateral macular degeneration having an appearance compatible with the Junius Kunt type was present, more advanced in the right eye. Visual fields demonstrated bilateral central scotomas.

General Physical Findings.—Physical examination was negative except for dermatologic changes. There was obvious loss of elasticity of the skin, with folds in the neck and axillae. Changes with ridges were also found around the mouth, all characteristic of pseudoxanthoma elasticum.

Laboratory Findings.—Routine laboratory examinations including determinations of serum calcium, phosphorus, and phosphatase, both acid and alkaline, were negative. X-ray of the skull was normal, although the carotid arteries in the region of the sella showed calcification.

Peripheral Vascular Findings.—All pulsations in the extremities were present, although in the dorsalis pedis and posterior tibial pulses of the left leg and posterior tibial pulse of the right leg were reduced.

Fig. 8.—Roentgen studies demonstrating calcification of the arteries in the thigh, lower leg, and foot.

Oscillometric studies showed that the oscillations on the left were one-half those on the right, which appeared normal. Vasodilatation test showed that the flow in both legs was within normal limits, although flow in the left was slightly diminished as compared with the right. Roentgen examination of the extremities showed moderate calcification of the arteries of the lower legs.

CASE 9.—A 45-year-old white woman was admitted to the hospital on June 4, 1954, because of failing vision in her right eye of two months' duration. She stated that shortly after 20 years of age she first noticed unusual folds developing in the skin of her neck and axillae. At approximately the same time she also began to suffer pain in her legs while walking, and during the previous five years she had noted precordial distress on exertion.

Ocular Findings.—Visual acuity was O.D. 6/60, O. S. 6/6, unimproved by correction. The eyes were healthy except for typical angioid streaks involving each retina (Fig. 9). Early changes of Junius Kunt type of macular degeneration were seen in the right macula, with elevation of the macular region and hemorrhages, both superficial and deep. The left macula was normal.

General Physical Findings.—The only abnormalities were marked changes of pseudoxanthoma elasticum occurring on the lips, neck, axillae, antecubital fossae, the popliteal fossae, and lower abdomen (Fig. 10).

Laboratory Findings.—Serum calcium, protein, albumin-globulin ratio, phosphorus, acid and alkaline phosphatase, cholesterol, and total lipids; urinalysis, and complete blood cell count were normal. Serologic tests were negative. Roentgen examination of the chest was negative. That of the skull demonstrated calcification of the choroid plexus (Fig. 11).

Peripheral Vascular Findings.—The right ulnar and the left radial arteries were oc-

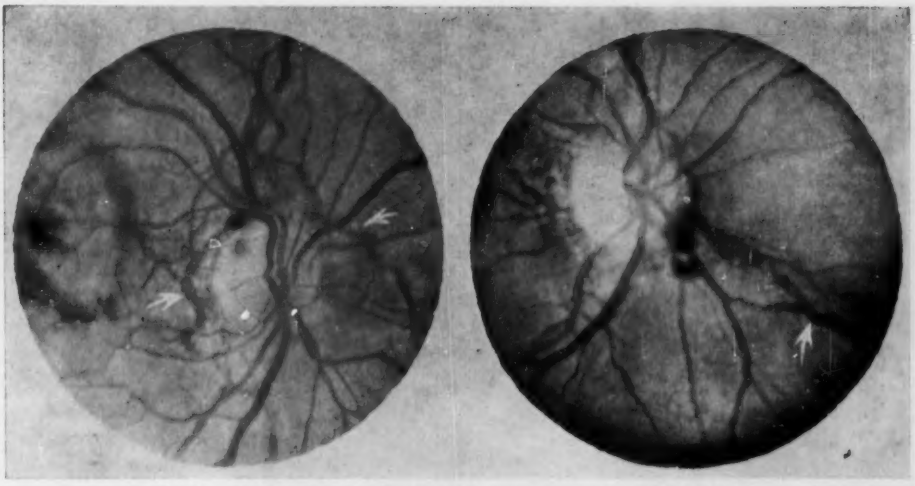


Fig. 9.—Fundus photographs showing typical angioid streaks, right and left eyes.

cluded. The right popliteal pulse was absent, and the left popliteal pulse was faint. Both dorsalis pedis pulses and posterior tibial pulses were absent. Vasodilatation test showed considerable reduced blood flow on the right, with less reduction on the left. Oscillometric tracings were markedly reduced at each ankle and only slightly less reduced at each knee. An ECG and an orthodiagram were normal. A vasodilatation test showed marked reduction in flow in the right leg and light reduction on the left. Ballistocardiographic studies were reported by Dr. Isaac Starr. He stated: "The record cannot be passed as altogether normal because one or two of the smaller complexes of the respiratory cycles are abnormal in form. The larger complexes of the respiratory cycles are altogether normal. Smoking did not make any difference in the record. In summary, while the record cannot be passed as normal, the myocardial abnormality is not very great. An E. K. G. gave a borderline tracing. Roentgen examination demonstrated calcification of the large artery in each thigh, in both lower legs and the right upper extremity."

Fig. 10.—Photographs showing typical changes of pseudoxanthoma elasticum *A*, about the neck; *B*, axilla.

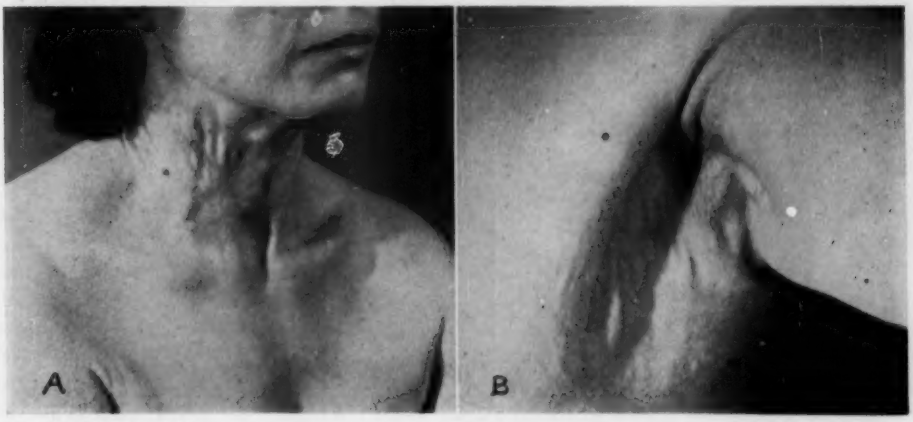


Fig. 11. — Roentgen study showing calcification of choroid plexus.

CASE 10.—A 60-year-old white man was admitted to the Veterans Administration Hopsital, Philadelphia, on March 22, 1955, because of pulmonary emphysema associated with mild congestive cardiac failure. He also gave a history of progressive loss of vision during the preceding four years.

Ocular Findings.—Visual acuity was O. D. CF, O. S CF. The vision was not improved by glasses. His eyes were normal except for the following fundus changes: Considerable pigment disturbance was seen around each disc from which typical angioid streaks radiated into the fundus. A rather

Fig. 12.—Photograph and x-ray showing characteristic picture of Paget's disease.

Summary of Findings in Ten Patients with Angioid Streaks

Case	Age, Yr.	Angioid Streaks	Macular Degeneration	Pseudoxanthoma Elasticum	Vascular Involvement					Paget's Disease
					Upper Ext.	Lower Ext.	Renal	Heart	Brain	
1	23	+	+	+	0	+	0	+	0	0
2	22	+	+	+	0	+	0	0	0	0
3	26	+	+	+	+	+	0	0	0	0
4	56	+	0	0	+	+	0	0	Aneurysm of internal carotid artery	0
5	45	+	+	+	+	+	0	0	0	0
6	44	+	0	+	+	+	+	0	Bilateral aneurysms of common carotid	Possible
7	63	+	+	+	0	+	0	0	0	0
8	55	+	+	+	+	+	0	0	Calcification of internal carotid artery	0
9	45	+	+	+	+	+	0	+	Calcification of choroid plexus	
10	60	+	+	0	0	+	0	+	0	+

broad angioid streak radiated temporally from each disc extending into the macular area, where advanced macular degeneration was seen. Visual fields demonstrated large dense central scotomas in each eye.

General Physical Findings.—The head was markedly enlarged and showed gross clinical evidence of Paget's disease (Fig. 12). The contour of the head was irregular. Veins of the scalp were markedly distended. The patient stated that he first noticed an increase in the size of his head at 18 years of age, which had been progressive. Marked kyphosis was present. His lungs were emphysematous. Roentgen examination of the skull and skeleton showed advanced changes of Paget's disease.

Laboratory Findings.—Routine laboratory studies including determinations of serum calcium, phosphorus, blood sugar, and blood urea nitrogen; urinalysis, and complete blood cell count were normal. Roentgen examination: Roentgen studies of the skull and long bones revealed a picture characteristic of Paget's disease, with rather advanced changes.

Peripheral Vascular Findings.—Peripheral vascular studies revealed a markedly reduced left dorsalis pedis pulse. There was also slightly low temperature response in the toes on heating the body. Vascular tone seemed normal. Roentgen examination of the extremities revealed calcification of an artery just below the left knee. Oscillometric tracings were moderately reduced in the left ankle and to a lesser extent in the right. An ECG showed evidence of myocardial disease. Both the right and left ventricles were involved.

Comment

Ten patients have been presented to offer further evidence of the close relationship between angioid streaks of the retina, pseudoxanthoma elasticum, and clinical signs of widespread vascular disease (Table). These patients, added to 1 previously reported by Ehlers and Marthinsen, 6 by Grönblad and Carlborg, 15 by Carlborg, and 2 by Scheie and Freeman, comprise a rather significant group now in the literature. There seems little doubt that the entity is due to a generalized degenerative process affecting elastic tissue throughout the body. The ocular, cutaneous, or vascular part of the syndrome may predominate.

All of the 10 patients reported in this paper had angioid streaks of the retina. Macular degeneration, often characteristic of the Junius Kunt type, was present in 8 of 10 patients, and the accompanying loss of central vision was the symptom which caused most of the patients to seek medical attention.

Pseudoxanthoma elasticum was evident in eight of the patients. One patient had advanced Paget's disease, and another had signs suggestive of Paget's disease.

Clinical evidence of arterial disease was present in all patients. Involvement was most marked in the lower extremities, where it was found to some degree in all of the patients. The arteries of the upper extremities were clinically involved in only six patients. Pulses were diminished or ab-

sent, and arterial occlusion of varying degrees was found. Oscillometric tracings were markedly reduced. X-rays of the extremities demonstrated calcification in many of the medium and larger-sized arteries. Intermittent claudication was a common complaint. Such advanced vascular disease in comparatively youthful patients was striking.

Evidence of cardiac disease and myocardial damage was found in three patients. One patient had an aneurysm of the internal carotid artery. Another had an aneurysm of each common carotid artery. Calcification was found in the walls of the aneurysms. Another patient showed calcification of the choroid plexus of the brain, and still another, calcification of the internal carotid artery. One patient showed bilateral calcification of the renal arteries, as well as the celiac axis.

The mechanism underlying the degenerative process is obscure. No disturbance in metabolism has been demonstrated. An hereditary element has not been detected.

In conclusion, the close relationship of the angioid streaks, pseudoxanthoma elasticum, and generalized arterial disease is emphasized. Since any part of the clinical picture can predominate, careful physical examination, with this disease in mind, should be carried out upon any patient with obscure arterial disease, especially if occlusive in nature, as it is obvious from some of our patients that the arterial disease can dominate the picture, or even occur alone, as can angioid streaks of the retina or pseudoxanthoma elasticum.

Summary

Ten patients have been presented to emphasize the relationship between angioid streaks of the retina, pseudoxanthoma elasticum, and clinical evidence of arterial disease.

The arteries of the lower extremities most frequently show clinical involvement, manifested by varying degrees of occlusion and roentgen evidence of calcification.

Arteries of the heart, brain, and kidney also show clinical changes.

This entity should be kept in mind for any patient with obscure arterial disease, especially if occlusive in nature.

Peripheral vascular studies were done by the Department of Peripheral Vascular Disease, Hospital of the University of Pennsylvania, Dr. Hugh Montgomery, Director.

313 S. 17th St. (3).

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Annual Reviews

Optics and Visual Physiology

ARTHUR LINKSZ, New York

A Partial Review of the Literature of 1956

Historical Notes, Introduction

This annual review is not in any way a complete enumeration of all papers which, in 1956, dealt with optics or visual physiology. Optics has become a science in itself, and the contents of magazines like the *Journal of the Optical Society of America* testify to the great diversity of material which all deals with "optics." Most of it is of no interest to ophthalmologists and beyond my grasp. Visual physiology is also a large field and, as a part of sensory physiology, is cultivated by both physiologists and psychologists, not to mention illumination and television engineers, colorimetrists, educators, and even physicists, artists, designers, and others, whose journals, unavailable to me, usually carry much of the material which could be labeled "visual physiology." This review is nothing but a record of the attempt of one ophthalmologist to keep up, without the benefit of a research or secretarial staff, with the progress of clinical optics and clinical visual physiology—the notes which one ophthalmologist has made of papers he could lay hands on, actually read, and abstract and which, after having been read, were filed under headings related to optics and visual physiology.

The 1956 review of these subjects will properly start with some reminiscing, as it was exactly 100 years ago, in 1856, that the first volume appeared of Helmholtz' "Handbuch der Physiologischen Optik," the book which, on the occasion of the centennial celebration of Helmholtz' birth, in 1921, by the Optical Society of America, Troland, its president, called "the Bible of physiological optics." The Optical Society once more took the occasion to celebrate Helmholtz' memory at this centennary. It also celebrated at the same meeting, aptly held in Philadelphia, the 250th anniversary of the birth of Benjamin Franklin, referring to the contributions of this great man to the science of optics (his suggestion of a wave theory of light and, of course, his invention of bifocals) among the host of his other contributions.

Unfortunately, no mention was made of another contribution to the science of optics, also exactly 100 years old and in its field also "epoch making." It was in 1856 that the Munich astronomer, Philipp Ludwig von Seidel, completed the series of his remarkable papers on the five aberrations of lenses —calculations without which design of modern optical instruments with large aperture and field demands would well-nigh be impossible. And in our fast-living era, even American ophthalmology has hardly noted that March 20, 1956, was the 100th anniversary of the birth of Edward Jackson.

No better introduction to the subject of visual physiology could be recommended than a publication by U. S. Office of Naval Research containing the proceedings of a Symposium of Physiological Psychology held at U. S. School of Aviation Medicine at the U. S. Naval Air Station in Pensacola, Fla. The symposium encompassed the whole field of physiological psychology, including taste, hearing, and the cutaneous sensations.

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The titles of the papers on vision and the names of their authors suffice to indicate the significance of this publication: Chemistry of Retinal Pigments, J. C. Peskin; Electrical Activity of the Human Eye, L. A. Riggs; Organization of Neural Activity of the Eye, H. K. Hartline and F. Ratliff; Stimulus Determinants of Speed in Classifying Visual Patterns, P. M. Fitts; Perception of Motion in Space, J. J. Gibson and O. W. Smith; Visual and Stereoscopic Acuity for Moving Objects, E. J. Ludvigh; Some Quantitative Aspects of an Opponent Color Theory, L. Harvich and D. Jameson; Sensitivity Changes During Adaptation to Illumination, R. M. Boynton. The interesting discussion of the individual presentations is also published, with introductory remarks by G. B. Newman. (The Proceedings can be obtained by writing to the Office of Naval Research, Department of the Navy, for ONR Symposium Report ACR-1.)

Another impressive publication of 1956 on an even grander scale contains the proceedings of the Florence conference on "Problems in Contemporary Optics," sponsored and organized by the *Institut Nazionale di Ottica*. There were six sessions devoted, in broad outline, to the following subjects: A. Optics and information theory; B. Nonclassical devices for image formation; C. 3-D and anamorphic systems; E. Aspheric surfaces; F. Optical problems of television; G. Retinal problems. Another session, D, was given to other "miscellaneous subjects."

In the session on retinal problems the greatest number of papers was read. Their titles (translated into English when given in some other language) and the names of their authors are as follows: On Mutual Interaction Between Both Eyes, M. A. Bouman; A Flicker Test for Foveal Interaction, C. Berger; Measurement of Visual Acuity as a Problem of Interaction of Retinal Elements, A. Kuhl; The Influence of Form Vision and Position Sense on the Measurement of the Minimum Separabile with Landolt Rings, H. Schober; Centrifugal and Antidromic Effects on the Retina, R. Granit; Rotatory Phosphenes Caused by Stimulation with the Alternate Electric Current, A. Manfredi; The Measurement of Rhodopsin in the Living Human Eye, W. A. H. Rushton; The Role of Stray Light in Glare and Contrast Phenomena, W. D. Wright; A Study on the Distribution of Light in the Retinal Image, F. Flamant; On the Influence of a Mydriatic on the Stiles and Crawford Effect, L. Ronchi; A Program of Research in the Visual Detectability of Distant Objects, S. G. Duntley and S. S. Ballard; Distribution of Sensory Units in the Extrafoveal Retina, M. Agular and J. Oliva; Remarks on a Phenomenon Described by Toraldo di Francia, A. Biot; The Influence of an Illumination Gradient and Its Variations on the Subjective Sensation of Brilliance, A. Fiorentini; Eye Movements in Relation to Retinal Action, R. U. Ditchburn; Studies on the Role of Small Image Movements in Relation to the Retina, A. Fiorentini and A. M. Ercoles; Psychovoltaic Reflex: A New Method of Objective Visual Sensitometry, A. Manfredi; Possible Interpretation of the Ultrastructure of Retinal Receptors Including an Electromagnetic Theory of the Primary Mechanism of Color Vision, E. Ingelstam; Reflex Actions of the Retina upon the Ocular Dioptric Apparatus, A. Ivanoff.

One will, of course, find papers within the field of visual physiology even in the proceedings of the other sessions. A masterly discussion by W. D. Wright in Session C dealt with "The Perception of Depth: The Relative Influence of the Monocular and Binocular Factors in Three-Dimensional Pictures." Another paper, by A. Arnulf, O. Dupuy, and F. Flamant, in Session C, dealt with "An Objective Method to Study the Defects of the Optical System of the Eye." And several papers given in Session F, such as "Physiology of Color Television," by the famous Yves Le Grand; "The Human Eye During the Viewing of Television," by G. A. Boutry, and "Flicker Fatigue, Light-Dark Ratio and Television,"

by A. Mahneke, obviously also dealt with problems belonging into the domain of visual physiology.

Since papers presented in such symposia are themselves often of the nature of a review and are presented for a special type of audience, their discussion will not be necessary in this place. However, this review would be even farther from its avowed purpose without making mention of them. The general session of the symposium was aptly dedicated to the optics of the 17th century Italian Jesuit Grimaldi, to whom another short reference will be found presently.

While it is not usual to note the birth of a new journal in an annual review, this opportunity should be taken to draw the reader's attention toward a new magazine, *Survey of Ophthalmology*, edited by Frank W. Newell, in which ample attention is given among the subjects of "Clinical Practice" to "Accommodation and Refraction" and in the section on "Basic Sciences" to "Optics" and "Color Vision." The main feature, however, to which special reference is due in just this review is the section "Classics of Ophthalmology" under the subeditorship of James E. Lebensohn, in which the reader will find reprints of such remarkable items related especially to optics and visual physiology as "Extraordinary Facts Relating to the Vision of Colors," by John Dalton, 1794; "Diffraction of Light," by Francesco Maria Grimaldi, S. J., 1665; "On Some Remarkable and Hitherto Unobserved Phenomena of Binocular Vision," by Charles Wheatstone, 1838, and "A New Discovery Touching Vision," by the Prior Edmé Mariotte, 1668.

Ophthalmologists will be pleased to have two papers on the chemistry of visual excitation from the pen of Professor Wald.[1,2] Both of them being essentially review articles, they also can only be mentioned here, and their perusal is warmly recommended. One of them, read at the Henry Ford Hospital International Symposium on Enzymes, naturally emphasizes this special phase of visual biochemistry, but it does it so lucidly as to make it easily understandable even to those looking for an introduction to the subject; the other, published in a volume on "Modern Problems in Ophthalmology," is meant as an introduction into the subject for ophthalmologists, and a part of its closing sentences is worthy to be quoted: "The neo-b isomer has not yet been found anywhere but in the eye and appears there to require special energy for its formation. . . . Yet it is the latter with which we see. It is difficult to avoid the inference that vision must gain something thereby—that what appears to represent so much needless difficulty must conceal some special advantage."

The publication in 1956 of the third volume, "L'Espace visuel," of Yves Le Grand's[3] monumental "Optique physiologique," can only be shortly mentioned.

Biochemical and biophysical research has in recent years contributed much to our knowledge of vision. Original papers on this subject are not meant to be covered in this review. Mention, however, should be made of an excellent short general survey by one of the chief contributors to this subject, F. D. Collins,[4] of the National University in Canberra. It was read to members of the Ophthalmological Society of Australia, and it contains a considerable amount of basic information condensed into 11 pages on matters like retinene and indicator yellow, the synthesis of rhodopsin and the isomers of retinene, vitamin A and A_2, porphyropsin, iodopsin, enzyme reactions, etc. It thus will serve as easily understandable general orientation to those needing introduction into the study of this phase of visual physiology.

Another basic survey dealing with the nature of the photoreceptor process, by Michaels,[5] will only serve those conversant with the mathematical treatment of biophysical processes.

Probably one of the most important contributions of the year to visual physiology in the stricter sense is a paper by Weale[6] which, as a summary of much of present-day knowledge on "Problems of Peripheral Vision," also does not lend itself to reviewing. Its study is urgently recommended to all

those interested in visual physiology. They will find that there are additional problems indeed to this phase of vision. First of all, the retinal image in the retinal periphery is of somewhat problematical nature, and both the transmission of light through the periphery of the cornea and the skew pupil and the diffraction of light on the latter become more complex as the light hits from obliquity. That the sensitivity of the retinal periphery is different from that of the fovea in both light- and dark-adaptation is well known. Still, it is amazing to find in this paper how many still unsolved questions there are. And the same is true of color vision in the periphery, several facets of which are also analyzed in this short monograph.

I. Electroretinography, Studies of Retinal Sensitivity, Adaptation, Flicker

The size and duration of the b-wave of the human electroretinogram (ERG) were shown by Johnson and Bartlett [7] to be dependent on the duration as well as the intensity of the stimulating light. Both, intensity and duration, share equally in determining the size of the submaximal b-wave until a certain critical duration is reached, which is about 100 milliseconds (σ) in the dark-adapted eye and less in light adaptation. Above this duration the size of the b-wave depends on intensity alone. Stimulus duration has no effect on the latency of response. (Interestingly enough, critical durations of just about 100σ have also been reported in psychophysical experiments.) The b-wave represents primarily activity of the scotopic system. This invites a search for parallels between the behavior of the b-wave and some characteristics of human vision, especially in dark-adaptation. The threshold recognition of a light flash in dark-adaptation follows an equation of intensity$\times$time$=$ constant, but only until some critical duration has been reached. The changeover is rather abrupt, around 100σ, in case the stimulus is restricted to small peripheral areas. A similar critical duration is a characteristic feature of experiments to elicit nerve impulses or to record ERG's in lower vertebrates. Of course, parallels are to be drawn with care. For a b-wave to be elicited requires greater flash intensities than the visual threshold intensity, and the sharp changeover in the latter occurs only on small areas, while the b-wave is a response to a diffuse stimulus.

Influence on the ERG of such stimulus factors as luminance, area, duration, and spectral composition have been studied before. Bornschein and Gunkel [8] analyzed the effect of still another factor, viz., that of the rate of change of intensity. They found that by altering the rate of the rise of light intensity the amplitudes of both the a-wave and the b-wave of the ERG are changed. By making stimuli rise slowly, the a-wave could be eliminated altogether, whereas the characteristic change of the b-wave was the prolongation of the response. Since earlier work by Johnson and Bartlett showed prolongation of the positive response by their increasing the duration of the stimulus, one will conclude that decreasing the rate of rise and increasing the duration of the light stimulus produce similar variations.

In his discussion of the work of Bornschein and Gunkel, Noell [9] emphasizes that many efforts to obtain "standards" for the normal ERG may be wasted because the instrumentation used by an individual researcher either has limited applicability or cannot easily be rebuilt in another laboratory. He suggests that the workers in this field first achieve some standardization of stimulus properties and then establish what is a "normal" response in terms of amplitudes, latent times, threshold, etc. The human ERG is, as Noell emphasizes, the sum of two potentials of opposite polarity with different latent periods of appearance, different time courses, and different stimulus-response relationships. The a-wave requires strong stimuli to be manifest, and the absence of it does not always indicate the total absence of a cornea-negative component. The time relationship of its latency period relative to the b-wave is subject to changes, and a slowly increasing stimulus might pre-

vent the a-wave from manifesting itself, just because the early fractions of the a- and b-waves cancel each other.

The ERG of 25 normal eyes and 50 eyes with ocular disease were studied by Iser and Goodman [10] (1) with the classic single-flash scotopic technique and (2) with photopic single-flash and photopic flicker techniques. Both scotopic and photopic ERG's are of greatest diagnostic value in disease conditions which involve selective ocular mechanisms, such as in congenital anomalies like color deficiencies and in heredodegenerative processes. In other types of retinal diseases, like chorioretinitis and retinal detachment, where selective involvement is not found, also in isolated lesions of the macula, photopic recordings add no new information. Photopic flicker stimuli offer more reliable recordings than responses to the single photopic flash method. Flicker electroretinography is therefore considered by the authors a useful adjunct to the standard scotopic single flash technique. They found that a standard frequency of 30 flashes per second is the most advantageous. Since in macular lesions photopic potentials are not different from those recorded in normal subjects, the photopic test has no diagnostic value. In retinal vascular pathology, retinal detachment, and chorioretinitis, if the disease is serious enough, scotopic and photopic potentials are equally depressed. The photopic ERG is of diagnostic value only where there is selective involvement. Two examples may be cited: With single flash scotopic technique alone a case of night blindness would have been falsely diagnosed as having severe retinal pathology. This was excluded by the photopic response, which proved to be normal. In another case of different nature, a totally color-blind subject with photophobia and 20/200 vision showed pathologic photopic but normal scotopic records, thus revealing a true nature of the condition. This subject was misdiagnosed to have a "learning problem."

Having published (in association with Dodt) some basic studies on flicker ERG in normal eyes previously, Wadensten [11] now deals with different pathologic conditions in which he feels that photopic or scotopic flicker ERG will contribute to diagnosis and differentiation of similar clinical pictures. He finds the method especially useful in differentiating damaged cone function, since in these cases scotopic single flash ERG (as introduced by Karpe) will be normal while flicker ERG is not. In other types of cases, single flash ERG might be fully extinguished and a flicker ERG, while not normal, might still be procurable. As examples Wadensten cites several cases of "primary" total color blindness in which a purely scotopic type of flicker ERG indicated normal rod function. One case was incorrectly diagnosed as amblyopia before being correctly placed by ERG. In "secondary" total color blindness related to heredoataxia and due to specific progressive retinal degeneration, the flicker ERG made possible differential diagnosis from descending optic atrophy. In cases of retinal venous or arterial occlusion the ERG gave no new information. In a case of quinine poisoning with tubular fields, a peculiar negative flicker ERG was obtained which the author considers to be a "practically pure" cone ERG. In retinal damage of not systemic nature (like posterior iridocyclitis, arteriosclerosis, retinal detachment) flicker ERG had no practical diagnostic value. Still it should be of interest that it could be elicited well even when single flash ERG was nearly or fully extinguished.

Henkes, van der Tweet, and van der Goss [12] used a method of selective amplification of the flicker ERG to achieve greater accuracy in the determination of the critical flicker fusion (CFF) and obtained higher values than with the simpler method. In several cases of primary degeneration of the retina, where the records showed a so-called extinguished ERG with the usual technique, this selective amplification produced the trace of a positive response.

In seven cases of uncomplicated retinal periphlebitis, François and De Rouck [13] found that the ERG was normal; in cases complicated by retinal proliferation or de-

tachment it was subnormal to the same degree as retinal degeneration had progressed. Even after the detachment was cured or the condition was stabilized, the ERG did not again become normal. The disturbance was especially evident in the diminution of the size of the b-wave.

A monograph by François, Verriest, and De Rouck [14] offers another example of the eventual practical usefulness of tests of seemingly purely theoretical interest for the intelligent diagnostic classification and the functional and etiologic analysis of ocular diseases. The cases studied belong to different groups of retinal degenerations classified into a peripheral group (such as pigment degeneration), a central and peripapillary group (such as macular degeneration or angioid streaks), and a cicatrical chorioretinal group. The methods of study included the photopic and scotopic campimetric field, adaptometry, tests of color vision (Ishihara, Farnsworth, Anomaloscope), electro-oculography and electroretinography. (An analysis of the results would be beyond the limits set for this review.)

Horsten and Winkelman [15] discovered a new phenomenon (called by them the "phenomenon of exhaustion"), consisting of the rapid decrease of the retinal b-potential on stimulation with repeated light flashes if the retina is under the influence of anoxemia. They first discovered this phenomenon on a patient suffering from chronic retinal anoxemia due to "thrombosis of the right eye," with 1/10 vision. They could also produce it experimentally on cats kept in an atmosphere of lowered oxygen concentration.

The effect of a new drug, nylidrin hydrochloride (Arlidin) upon the b-wave of the human ERG was studied by Jacobson and Basar.[16] Their subjects were dark-adapted for 25 minutes, and their base-line ERG was recorded. They were then given 12 mg. of the drug, the ERG's were recorded at intervals up to 30 minutes, and the amplitudes of the b-waves were calculated in terms of per cent increase over the base-line value. The authors conclude that the drug caused increase in retinal blood flow of over 32% and that "it may be inferred that nylidrin increases cerebral blood flow."

A paper by Barlow [17] is of interest more for the theoretical concepts it introduces than for the experimental material it offers. The rather striking term "retinal noise" in its title can only be understood in case one knows of the newer connotations of the term "noise" in communication engineering. In this sense of inevitable random activity, "noise" in the retina and optic pathways is a limiting factor of the ultimate sensitivity of the eye to light and, therefore, influences the magnitude of the absolute threshold. Thus, even if one quantum of light should be sufficient to excite a retinal rod, excitation of one rod could not be differentiated by the central nervous system from retinal "noise" and at least two or possibly more simultaneously excited rods are needed to give a threshold sensation of light.

Popp and Durchschlag [18] found that intraocular ischemia of 30 seconds duration produced by compression of the eyeball with the ophthalmodynamometer caused a drop in sensitivity with restitution of normal values within a few minutes. This initial drop was followed by a secondary reduction of sensitivity of considerable duration. The sudden loss of sensitivity is taken by the authors to be the expression of a synaptic block, while in the secondary reduction of sensitivity they see the influence of ischemia on the ganglion cells of the retina. There is no reason to assume that ischemia has any influence on the photochemical aspect of sensitivity (the process of adaptation in the strictest sense), though it greatly hinders the influence of light upon the adaptation process.

In a paper of rather polemic tenor, Verhoeff [19] reiterates once more his belief that Moore's lightning streaks have no serious portent. "Judging in addition by what is now known as to their cause, they can even be accepted as constituting a good omen for the affected eye." Verhoeff believes that "when a patient complains of lightning streaks and does not already have retinal separation in the affected eye, this danger

from shrunken vitreous has largely if not wholly passed."

After initial light adaptation to white light of 150 millilamberts luminance, Polinsky and Young [20] exposed the eyes of their subjects to a secondary preadaptation procedure with colored filters (Wratten No. 25 for red, B2 No. 58 for green, and C5 No. 47 for blue), the lights being so adjusted as to provide equal luminance (16 millilamberts) through the filters. This secondary preadaptation lasted 2, 3½, 5, and 10 minutes. The effect of this preadaptation on the course of the following dark-adaptation period was determined in a Hecht-type adaptometer. Red was found especially effective in reducing the time required to see the lower luminance values. Blue had little effect, while that of the green light was halfway between that of blue and red. However, for the final adaptation to the lowest luminance levels, green was about as effective as red. Since the three hues were equated photometrically, one must conclude that each group of wavelengths had a different effect on the scotopic mechanism. Both the red and the green filters were found to be maximally effective after three-and-one-half minute exposures. They were still sufficiently effective after five minutes. This is of practical importance to know for those who want to wear preadapting colored goggles in order to save on dark-adaptation time. Counting the dark-adaptation time required to reach some standard threshold level (say 4.44 log micromillilamberts), more time is saved by wearing the preadapting red goggles for three and one-half minutes than with any other length of time. In this case it takes about 13 minutes to reach the required level. After red goggles have been worn for 10 minutes, still another 11 minutes are needed. Thus the latter preadaptation procedure is less economical, if saving time is of the essence.

Fang, Hall, and Hwang [21] showed that foveal dark adaptation increases even after a constant level has seemingly been achieved. The threshold after 8 to 10 hours is about one-half of the one-hour threshold. This additional increase, the authors feel, cannot be due to further photochemical regeneration but must be due to nervous or cortical factors.

Differential sensitivity between two spatially separated homogenous fields was measured by Hake and Averbach [22] with (*a*) the two fields separated by darkness and (*b*) the two fields joined by a transition area. Detection was significantly better with the gradient present than with separation by darkness. The visual system is thus able to utilize the distribution of light in an intervening gradient to emphasize the differences in luminance in two separated fields.

Studies of the "light sense" give, according to Busch,[23] earlier and more accurate prognostic hints than the study of visual acuity in operated on cases of retinal detachment. Even the beginning of a relapse can be prognosticated by light sense determinations, a fact of especial significance when the ophthalmoscopic picture is not unequivocal. With the same relatively poor visual acuity, poor light sense means poor prognosis and good light sense, good prognosis. The main problem with light sense studies is their complexity. For the successful performance of threshold studies at the bedside, present-day technical methods would need considerable simplification. Busch describes two simple procedures for the comparative study of the light sense under clinical conditions. In the first, he uses the Zeiss hand ophthalmoscope and compares the distances from which the patient calls the light equally bright when falling on the normal and on the operated on eye (e. g., if the distance is 1 m. for the good eye and 0.5 m. for the other eye, he calls the light sense "¼"). In the other procedure he uses one of the old-type ophthalmoscope lamp housings with the variable Aubert stop. A light source of known brilliance is used, and the opening of the Aubert stop is regulated. Using, for example, a 2×2 mm. opening, Busch found that normal eyes recognize the presence of light after one-half-minute dark adaptation from about 7 m. This he calls light sense "1." If the operated on eye

recognizes the presence of the same light source from only 2 m., the light sense is $(2/7)^2$, i. e., about "1/13." If it recognizes the presence of light at only 1 m. and only after opening of the stop to 8×8 mm., then the light sense is $(1/7)^2 \times (2/8)^2$, i. e., about "1/800," and so on.

Busch also uses this method in cases of complicated cataracts, after perforating injuries to see if the eye is worth saving, in pigment degeneration, in disseminated choroiditis, and in other cases. (The procedure is, no doubt, a crude one, but until better instrumentation of clinical usefulness is available it certainly is worth remembering.)

Granger [24] tested 100 neurotics and 40 normal controls, determining, after a period of light adaptation to standard luminance, the time required to perceive the position of a faintly illuminated object. He believes that he has proved that neurotic patients need longer "perception times" than normals and offers several hypotheses as a possible explanation of his findings. According to him, it is conceivable that "regeneration of visual purple may be impaired in certain psychiatric patients as a secondary effect of somatic neurosis. . . . The possibility of impairment of the nervous mechanism (of the retina) provides another possible type of explanatory hypothesis." Since it is known that the excitation-inhibition balance of the retina may be modified by chemical agents such as epinephrine, the apparent impairment of scotopic thresholds in neurotics may also be due to "excessive activity of the sympathetic nervous system." Moreover, "adrenalin may also exert an inhibitory effect on the visual cortex." Finally, he feels that one has "to consider such factors as attitude, judgment and attention . . . an impairment of 'higher-level' processes."

While most research workers naturally pry for new knowledge, relying on established standards of performance as a basis of comparison, it will always be useful if the standards themselves are sometimes restudied. Such is the work published by Dieterle and Gordon,[25] who examined the standard curve of dark adaptation and its physiologic limits with the Goldmann-Weekers adaptometer. This is a photometric precision instrument and is so constructed that one can record the logarithm of the light threshold for a given time directly on paper attached to a drum which makes one rotation per hour. Since dark-adaptation curves of different persons are never identical and vary with method, it is important that a standard technique be used and that the standard curve and the physiologic limits for a new instrument be known. Only with this knowledge will it be possible to evaluate pathologic findings.

The Goldmann-Weekers instrument was found useful by Miller [26] in a study of dark adaptation of patients with glaucoma and the possible influence of acetazoleamide (Diamox) upon this function. At first, a base-line curve was established, and then administration of the drug was begun and dark-adaptation was studied repeatedly over the course of treatment, of as much as 5 to 18 weeks. It was found that dosages of 0.5 or 1 gm. a day did not adversely affect the dark-adaptation function of these patients.

That the tools and methods used by students of retinal physiology finally increase clinical understanding is beautifully illustrated by an important paper by Zeavin and Wald.[27] A specially built perimetric adaptometer enabled these authors to study the functional status of rod and cone vision in the surviving retina of persons afflicted with pigment-degeneration of the retina. Their instrument makes it possible to determine the threshold of rod or cone vision with light stimuli of known and specified dominant wavelength—580 mμ for cone vision, 520 mμ for rod vision—in any desired area of the retina up to 70 degrees from the fixation point. The studies could be executed across any desired retinal meridian, thus offering a set of profiles of retinal function and a definite index of the course of the disease. Moreover, a standard to study the possible influence of therapeutic agents could finally

be established. Compared with their normal configuration, these profiles were found totally inverted in the case of pigment deterioration. The fovea retained its normal threshold, while thresholds in the periphery might have risen as much as 4 log units to a level much higher than that of the fovea. Many areas of the retina seemed to retain characteristics of cone vision even well peripherally, where usually rod vision prevails. Especially interesting were the dark-adaptation curves for white light as determined at different distances from the fovea. At 5 degrees above the fovea adaptation curves turned out to be duplex, showing that both rods and cones are present. The normal level of the cone plateau indicated a normal complement of cones, while the high rod plateau indicated damage to rod function. Ten degrees from the fovea curves were simple, rod function being apparently absent, and the cone threshold itself was also higher than normal, indicating damage to cones as well. The spectral sensitivity curves of these eyes (measured in dark adaptation) were displaced about 10 log units above normal level, indicating general retinal deterioration. Still, at 5 degrees from the fovea both orange and blue stimuli gave the typical rod sensitivity curve, while 10 degrees from the fovea typical cone curves were obtained. Even in the early stages of the disease, the entire extrafoveal area seemed to be abnormal, while pigment appeared only in the more degenerated areas. Every case of pigmentary degeneration seemingly starts with a *sine pigmento* state. The initial site of the attack of the disease is in the rods, especially in those within 25 degrees from the fovea. Only late does the degeneration spread more peripherally. The peripheral cones outlast the rods, later degenerating themselves. The fovea remained normal into the last stages the authors could study.

Of the many factors which influence the perception of flicker and the flicker fusion frequency (FFF) or critical frequency of flicker (CFF), some were once more analyzed by Collins.[28,29] His papers are purely technical, though published in the *Ophthalmologica* and come from the Building Research Station of the Department of Scientific and Industrial Research in England. They are beautiful examples of basic research done in an industrial laboratory and with a view toward practical application of results. The classic results of Lithgoe and Tansley were confirmed, and we learn once more that for small test stimuli and at photopic levels of luminance CFF increases whenever the luminance of the surround is raised. The linear logarithmic law of Ferry and Porter which governs CFF was found to hold for all the variations of the examined wave forms and up to luminances of 50 ft-lamberts on small fields and 300 ft-lamberts on larger fields. CFF, plotted logarithmically, was found to be a linear function of average stimulus brightness, increasing with the "modulation"

$$\left(=\frac{\max-\min}{\max}\right)$$

and also with the "light-time ratio." It was also found to increase, but not linearly, with increase of field.

All this reevaluation was undertaken with the purpose to estimate the probable level of complaints of flicker that can reasonably be expected whenever people work under discharging lamp installations of various physical characteristics. In England and over most of Europe the fluctuation of light from fluorescent fixtures is 100 cps. This frequency is the second harmonic of their mains frequency, which is 50 cps. Fixtures of this type, if producing luminance of the order of 100 ft-lamberts on the general surroundings, are very unlikely to cause complaints of perceptible flicker under correct installation conditions. Some lamps, however, show a superimposed subharmonic of 50 cps. Amounts up to 10% of this subharmonic were found in new as well as in old lamps examined for wave form, and the most likely cause of complaints due to flicker at normal levels of illumination is the presence of this subharmonic of sufficiently low frequency.

Further experiments were therefore carried out to determine the relative amounts of it and the various degrees of flicker discomfort at different levels of luminance. As the proportion of the subharmonic increases with luminance, it can be expected that under high illuminations and luminances over 20 ft-lamberts some of the subjects experience discomfort. Its presence in large enough amounts is "sufficiently common to account for the majority of genuine complaints which have arisen." The usual frequency of fluorescent light causes no discomfort.

Renewed attention was called to the clinically significant aspects of the study of CFF by Hylkema.[30] Its usefulness is beyond question, and its determination for clinical purposes deserves to become more popular. "It is a form of quantitative perimetry that has many advantages. It is possible to determine accurately the function of the organ of sight in the entire visual field and express it in numerical terms." Various factors, however, influence CFF, and they should not only be taken into account but carefully enumerated when results are reported, since under different conditions of investigation the numerical results are also different. Of the clinical examples offered by the author, some are worth mentioning. In glaucoma, flicker perimetry is a sensitive method for detecting scotomas. After CFF has been determined in the center, the frequency of interruptions of light should be slightly raised and the light projected at several other retinal areas. If the eye is normal, flickering should be experienced everywhere except in the center and the extreme periphery. (Obviously, Hylkema finds with his instrument and his technique that CFF is lower in the fovea than in the periphery. Others, to be sure, report different results.) In optic nerve atrophy and optic neuritis, changes of CFF will indicate whether the condition is improving or progressing. Amblyopia can be differentiated from retrobulbar neuritis by this test, as in the former condition centrally determined CFF is higher in the affected eye than in the normal eye (this is again not found by other investigators), while the opposite holds for retrobulbar neuritis.

Indeed, as Mahneke[31] emphasizes, procedures to investigate CFF have not yet been standardized and thus the results of different investigators often appear to contradict each other. The most frequently used technique is actually over 100 years old. It was introduced by E. Schafhäutl in 1855. He kept the stimulus brightness constant and changed the frequency of light flashes. The reverse principle, that of keeping the number of flashes constant while changing their brightness, was used by L. Goldberg (1943). He found the latter technique a better indicator of CFF. Using this technique, there are of course still two different ways to determine the value of CFF, viz., by measuring the transition from flicker to fusion or the opposite. The first technique is known as *d-c* (discontinuous-continuous); the latter, as *c-d* (continuous-discontinuous). The two values do usually not coincide, and authors therefore are in the habit of using their arithmetical mean as the CFF value. Furthermore, the measurement can be done in a continuous fashion, letting the subject look at the flickering object throughout the time required for the threshold determination, or in a discontinuous manner, presenting the stimulus in consecutive brief exposures only. A further variable factor is the rate of acceleration or deceleration. Finally, the starting points of the determination may vary. In an extremely valuable and easily understandable study on the significance of all these factors, Mahneke analyzes the effect of the rate of acceleration on both the *d-c* and the *c-d* values of CFF. He found that the *c-d* threshold is independent of changes of rate of acceleration, while the *d-c* threshold is not. With low accelerations the *d-c* threshold was lower than the other. The two curves met at acceleration values of about 5 cps, and at higher acceleration values the *d-c* threshold becomes actually higher than the other.

Critical flicker frequency was determined by Feinberg[32] at four retinal positions (8 degrees nasally and foveally and 8 and 24

degrees temporally) in normal control cases and in three cases of amblyopia ex anopsia on both the normal and the amblyopic eyes. The values of the mean for normal eyes were 25.9 in the fovea, 16.9 and 16.2 at 8 degrees temporally and nasally, and 15.7 at 24 degrees temporally. In the amblyopic eyes the foveal mean critical flicker frequency value was 16.1; the values at 8 degrees temporally and nasally were 17.5 and 16.0, and at 24 degrees temporally the value was 16.9. In marked contradistinction, the normal eyes of the same subjects revealed foveal peaks similar to those of the normal eyes of the control subjects. The subjects thus showed marked and statistically significant depression of CFF in the foveal area of the amblyopic eye, paralleling the depression in their visual acuity. This result, according to the author, argues against some current views which postulate that in amblyopia ex anopsia pattern vision is selectively impaired, and it contradicts the classic and much-cited findings of Teraskeli, who claimed the CFF to be consistently higher 10 degrees temporally than in the fovea, with a reduction of this difference in amblyopic eyes owing to a relative increase of their foveal CFF. A similar decrease of the difference between peripheral and central CFF was found by Miles. Feinberg concludes that there exists a deficit in light perception in amblyopia which tests of absolute threshold, spectral sensitivity, and dark adaptation (Wald and Burian) fail to reveal but which is shown by the technique of intermittent retinal stimulation.

Flicker-fusion-threshold and choice-reaction-time measurements were made by Landis, Dillon, and Leopold[33] on a group of psychiatric hospital patients before electroconvulsive therapy (ECT), during the course of treatments, within 24 hours after the last treatment, and at intervals of 2, 3, 4, and 6 weeks after the last treatment. At each occasion, each patient was tested twice, first without and then with one of three "physiological loads." These loads were (1) intravenous injection of hexobarbital (Evipal), (2) 0.4 mg. glyceryl trinitrate (nitroglycerin) sublingually, and (3) the cold pressor test (hand submerged in ice water). Both measured quantities were significantly affected during the course and at the end of ECT and for another two weeks after the last treatment. The physiological loads did not add significantly to the injury caused by the treatment, except for the absorption of glyceryl trinitrate, which possibly affected choice-reaction time during and after ECT.

In patients with retrobulbar neuritis, Kurachi and Yonemura[34] measured the CFF in the region of the scotoma. In normal subjects, CFF increases in logarithmic fashion as area of stimulation increases (Granit-Harper law); in patients with retrobulbar neuritis no such increase was observable. Similarly, the increase of stimulus intensity also had no effect in these cases, while CFF increases with stimulus intensity in normal persons. The same type of difference from the normal was observed in two cases of typical congenital achromatopsia. This similarity of behavior, as well as the poor visual acuity prevailing in both conditions, suggests to the authors a similarity in the underlying pathology and makes it at least a possibility that the block to visual nerve impulses in so-called retrobulbar neuritis is in the retinal neuronal network, the bipolar-cell layer, rather than behind the globe (as has generally been assumed).

II. Illumination, Glare

An excellent short review of what ophthalmologists should know about fluorescent lighting and its effects on the eye was read before the Ophthalmological Society of Australia by Dresler,[35] of the Commonwealth Department of Labour. He discussed the types of ultraviolet radiation (called A, B, and C) and their presence in fluorescent sources of light, the spectral composition of these sources and their distorting effect on color rendering, the ocular chromatic aberration associated with them, the sometimes disturbing stroboscopic effects and actual flicker, and the types of glare caused by

faulty application of these sources. It turns out, from this analysis, that the alleged harmful effects of fluorescent lighting are purely imaginary. Ultraviolet A has the longest wavelength, reaching down to about 320 mμ; it is absorbed by the crystalline lens and tans the skin without burning it. The B range is between 280 and 320 mμ and is responsible for erythema and photophthalmia. The C range extends below 280 mμ and is rather active in a harmful way, even causing coagulation of albumin. Fluorescent lamps generate a considerable amount of C, but this is absorbed by both the powder lining and the tube and the amount that escapes is too small for harmful effect. The amount of ultraviolet light in the B and A ranges emitted by these lamps is about 150 times less than that received from midsummer sun. Answers to the faulty color rendering are readily available, and some modern types of luminaries in fact emit sufficient red light to correct for the faulty color temperature of the other types. Stroboscopic effect and flicker can be largely corrected by multiphasing and the avoidance of large areas of high brightness in the immediate surround of the visual task. Glare can also be eliminated. These are technical problems, beyond the competence of the ophthalmologist. All he has to know is that it is not impossible to eliminate any or all sources of discomfort. Individual tolerance, of course, is a factor. In warm fluorescent light of about 60 ft-c., hardly 1 of 150 persons will notice the inevitable flickering of certain portions of the discharge, while four or five times as many will notice it with the other type of bluish light.

A report by Dejean[36] on the effects of lighting on the eyes is not so encouraging. What with the more excitable French temperament, all kinds of nervous upsets from burning eyes to epileptiform attacks are traceable to the flickerings of fluorescent lights, while its different shadings of color might make a person calm (green), irascible (orange), or at peace (violet). We also learn of the persistent irritability, nervous reactions, sourness of character, and aggressiveness of the workers in factories making photographic products—all assuaged by the change from red illumination to green. The paper ends with the fine suggestion that for a good desk lamp incandescent lighting is still preferable.

A booklet[37] called Recommended Practice for Office Lighting, prepared by the Illuminating Engineering Society's Committee on Office Lighting, includes the results of consultations over the past years with representatives of the I. E. S. Committee on School Lighting, the American Institute of Architects, and the National Council for Schoolhouse Construction. It is worth having and reading and can be obtained for 50 cents by writing to the Society.

Glare, according to Hopkinson,[38] can result (1) whenever the whole or nearly the whole field is excessively bright or (2) whenever light from a small source hits the retina while the surround is so dark that under the given conditions the brightness of the source is beyond the temporary adaptation range. (The intensity of the light source might at the same time be well within the absolute adaptation range of the eye: Automobile headlights, which are intolerable at night, hardly disturb in daytime.) The uncomfortable sensation of glare may at least in part be associated with the opposing actions of the sphincter and dilator of the pupil. These are due to the instability arising from contradictory irritations, since parts of the retina are stimulated from the less fully illuminated parts of the visual field, while others are illuminated by a glare source of high luminance. No clear relation between the pupillary diameter and the magnitude of the glare sensation could, however, be established.

Kittel[39] differentiates between a dioptrically conditioned feeling of "glare" and real "photophobia" and finds four different groups of conditions in which photophobia is a symptom: (1) inflammations of mucous membranes of nose and eye and of the cornea; (2) iritis and iridocyclitis, which may cause it even in the other, nonafflicted, eye; (3) diseases of the retina

and optic nerve; (4) central disturbances such as meningitis and encephalitis. The primary cause is, according to this author, an abnormal sensitivity of the vegetative centers in the midbrain with afferent paths in the trigeminal and optic nerves. Drugs which influence photophobia favorably, such as atropine and naphazoline (Privine), have a local effect upon the primary disease process, causing a secondary diminution of centripetal stimuli.

III. Color Vision and Its Defects

A definite yardstick to measure colors was developed by W. R. J. Brown, of Eastman Kodak Research Laboratories. He received the Adolph Lomb Medal of the Optical Society of America for these studies leading to an exact method of determining shades of color. Brown and his associates [40] used 22 basic colors and made a total of about 17,000 matches on a great number of color-normal persons. There are, according to these investigators, more than 20,000,000 different shades of color which can be seen by the normal eye. And these studies, to Brown's and his associates' satisfaction, prove once more the trichromatic nature of human color vision.

A trichromatic colorimeter of rather simple design was developed by Bouman, Walraven, and Leebeck.[41] Such a simplified instrument might possibly be used in mass tests for personnel selection. Its designers believe that it offers more quantitative information than the usual pseudoisochromatic plates and that it has a larger diagnostic range than the anomaloscope. One will have to wait until actual measurements on a sufficient number of subjects have been made before it will be apparent whether or not this instrument meets expectations. The need for a simple and not too expensive colorimetric device is certainly great.

In a mass testing procedure in Australasia, Mann and Turner [42] found that among the white Australian males tested with the Ishihara plates (edition not mentioned) 7.3% had defective color vision. For females the value was 0.61%. For "colored" (half-caste) people the respective numbers were 3.2% and 0%, and for the aboriginal population, 1.9% and 0.03%. These latter figures are the most accurate, since a large sample was tested. "There is no ground for supposing that primitive races have less good color vision than people of European stock." On the contrary, their color vision is likely to be much better. (Earlier studies by Geddes with the Ishihara test among the Fiji showed similar results, while among Indian male residents of Fiji color deficiency amounted to 8.1%. Still earlier studies by Rivero on the Papuans revealed not a single case of color blindness.)

Shlaifer,[43] experimenting with artificially created blurring of retinal imagery, found that color is differentiated at worse levels of fogging than form. He noted, besides, that greater amounts of fog were needed to eliminate color discrimination binocularly than monocularly. This suggests to him the existence of some kind of binocular reinforcement in the discrimination of color.

Having published an evaluation of a pilot model of the Hardy-Rand-Rittler (H-R-R) pseudoisochromatic test some time ago, Rand and Rittler [44] (after the untimely death of the senior creator of the test) made it their task in their newest study to evaluate the commercially available plates. The evaluation was carried out on 154 boys, age 12 to 18, of a small private school. The devices used for comparison were the AO Revised Selection approved by the I. S. C. C. Subcommittee on Color Blindness, the fifth edition of the Ishihara plates, and the Boström-Kugelberg plates. Out of 154 boys, 11, or 7.14%, were found to be defective on both the AO Revised Selection and the evaluated plates. Also retested was another sample of 97 color defectives examined previously with the pilot model and the AO Revised Selection. At that time the two tests agreed in 96 cases. Only one subject was classed as defective by the older selection and not by the newer test. However, the H-R-R test was designed not so much to detect the presence (for this there are sufficient office tests) but also the degree of

the color defect and to classify the defect. The retest study showed a "strong agreement" between both the qualitative and the quantitative classifications offered by the two editions. Studying the tables, one finds that the agreement was better in the qualitative classification, while there was a small but significant percentage of cases classed as medium defective by one edition and strongly defective by the other. This, however, is understandable. The separation of defectives into three groups (mild, medium, strong) must be, by the nature of things, somewhat arbitrary, and borderline cases will occur, which sometimes are fitted into one, another time into another, category.

Steinmetz and Kearns [45] found the AO H-R-R test "a simple, useful aid in the diagnosis of past episodes of acute or chronic retrobulbar neuritis of multiple sclerosis." When other residual signs or pallor of the optic disc are present after an episode, the test was found a dependable means of confirming the diagnosis. In other cases in which the visual acuity, optic discs, and visual fields were normal, the plates often gave the only objective evidence of past involvement with retrobulbar neuritis.

Sloan and Habel [46] investigated the efficiency as a screening test of the Dvorine plates, a new edition of the Ishihara plates, the new AO H-R-R plates, and a new set selected by them from four different American and European compilations (referred to as the 20-plate test). Deficient color perception was also confirmed with the anomaloscope, the Color Threshold Tester, and the two Farnsworth-Munsell procedures. The AO H-R-R test turned out to be slightly inferior to the Ishihara and Dvorine tests because of its occasional misqualification of normal subjects. Each of the tests was also found occasionally to fail to detect mild degrees of red-green deficiency. Analysis of responses to individual plates of each series indicated that in order to detect borderline cases certain test plates of all the tests should be modified in such a manner as to become more difficult for the color-deficient observer. The occasional misclassification of normal subjects by the AO H-R-R test could be reduced best by an increase in the number of screening plates (which only number four) and the adoption of a less stringent passing score (the number of failures permitted is zero). On the other hand, the authors feel that the AO H-R-R test, giving information as to the type and degree of the defect, is more generally useful than any of the other pseudoisochromatic tests.

The new (1953) edition of the aptitude test of the Inter-Society Color Council is the subject of a study by Dimmik.[47] The new edition follows the pattern of the earlier (1944) one. It is a matching test in which the examined person must find the duplicate (in both hue and saturation) to samples of four basic colors set in random manner upon an easel. Great care was exercised during the production of the color samples, and so there is every reason to believe that data obtained with one set in a given batch of sets will not materially differ from those obtained with any other set.

More interesting for the ophthalmologist than the purely technical statistical data published in this paper are the comments made on it by Walls (*Survey Ophth.* 1:495-496, 1956). This expert warns practitioners against considering themselves as willing to measure color aptitude as they are ready to test for color blindness. A color aptitude test means an exhausting job for both examiner and "testee" and should properly be performed by a trained technician or colorimetrist. "Color aptitude" is the ability to see a color difference between color stimuli which differ only slightly. This ability is not necessarily good, even in a color-normal person. It has nothing to do with the usually measured ability to discriminate differences in hue. In other words, it is not a test for color blindness or the absence of any color "deficiency." The ability tested is that of detecting small differences in the purity of samples when there is no difference in hue.

The spectral neutral points of protanopes and deuteranopes were determined by Walls

and Heath.[48] They used in the beginning the CIE Illuminant C of 6500 degrees K and turned later to the NBS Illuminant D of 7500 degrees K. Neutral points were determined by mixing blue and green Munsell paper discs by means of a rotary color mixer. With Illuminant C, the neutral point range of protanopes covered 3.7 mμ, with 492.3 mμ as the mean; the range for deuteranopes was 5.8 mμ, with the mean at 498.4 mμ. With Illuminant D the respective ranges were 3.3 and 5.1 mμ, with the respective means at 490.3 and 496.2 mμ. Between the two groups a definite gap was evident. "It is therefore possible, after all, to tell a protanope from a deuteranope by the location of his neutral point." Ever since the studies of Pitt (1935), the wavelength at which $\Delta\lambda$ is minimal is assumed to be the neutral point of the protanope or deuteranope. It is here that the dichromate exchanges one of his two existing hues for the other. It is not only because of maximal desaturation but also because of this hue change that he is at this point so very sensitive to a small change of wavelength. These true neutral points were determined by Pitt at 490 and 494 mμ, respectively, values which are closer to those found by the present authors with Illuminant D. This speaks for the use of Illuminant D rather than Illuminant C as the "true white" in physiologic work. Another reason for this preference is drawn from the subjective description of color by the tested subjects. None of them called Illuminant C "blue" or "bluish," although color-blind persons are able to recognize this color. On the contrary, several of the authors' subjects called this illuminant greenish or pinkish, which names must not be taken too literally but obviously mean that the subjects found Illuminant C not neutral and especially not being beyond the neutral point. There was no suggestion that Illuminant D was found too bluish. It is, according to the authors, the best illuminant so far to be assigned as the "physiological white standard."

Another method to separate deuteranopes from protanopes might have become feasible through the very meticulous measurements of the state of dark adaptation by Remberg.[49] These enabled him to study the individual peculiarities of the Purkinje shift, which, in the protanope, turned out to be so different from that of the deuteranope that the difference itself becomes useful in differentiating between the two conditions.

Stams[50] describes the case of a 40-year-old man who, after having been stricken with epidemic typhus, became almost totally color-blind, showing only remnants of the sensation of blue. His visual acuity was correctible to normal. His fundi, binocular functions, and visual fields were normal. Dark adaptation and perception of light were definitely diminished. Since the ophthalmologic history of the patient before his disease is known, the case is unquestionably one of acquired color-vision deficiency. Stams assumes the disturbance of color vision to be central (or cortical) in origin, though the disturbances in dark adaptation speak for a lesion in the lateral geniculate body, or even more peripheral structures. His analysis of the case reveals full red-green blindness and severe disturbance of the yellow-blue mechanism. Even blue was only recognized in high saturations.

The patient was carefully studied with skeins, Stilling and Ishihara charts, color discs, several types of anomaloscopes, and the Trendelenberg method of colored specks. In the latter test, blue was correctly named in high saturations. Monochromatic lights were not recognized, except in the region 442-482 mμ, where they were definitely called blue, and up to 485 mμ, where they were called bluish. No other color was recognized. Since this is a case of acquired color blindness, it is permissible to use a color-naming process. In case of congenital disturbances naming of colors has many pitfalls.

The most prominent member of an unusual pedigree of color defectives collected

by Crone[51] is a 41-year-old woman with atypical cone monochromatism who seemingly derived her remarkable color defect from a combination of deutero and trito factors. One of her sons is deuteranomalous. Another son is also a monochromate (even if incompletely). One will, in his case, assume a deutero defect and a less marked trito defect. A sister of the woman has color amblyopia, and Crone thinks her to be heterozygous for deuteranopia, having a factor for trito defect at the same time, like many other members of the family. This sister has one normal daughter, one daughter who is tritanomalous, and a son who is a deuteranope. This son shows low wavelength discrimination in blue and thus must have a factor for a trito defect besides the deuteranopia. Another sister of the first-mentioned case is a deuteranope and has two typically deuteranomalous sons and two normal daughters. A female first cousin of the first-mentioned woman (the fathers are brothers) manifests severe disturbance of red-green discrimination, indicating the presence of a trito factor. Another male cousin of the same woman (her father's sister's son) has an isolated trito disturbance, a kind of incomplete tritanopia. She herself was the subject of a previous publication by Hylkema. This author examined the two sons of this woman when they still were very young. His diagnosis (that one is a protanope, the other a deuteranope) was not substantiated by Crone, who therefore cannot agree with Hylkema's assumption that the mother was a compound heterozygote of deuteranopia and protanopia. Crone thinks that the atypical monochromatism of this woman is due to a combination of deutero and trito defects. (Another analysis of this unique case is to be found in a paper by Walls.)

In the dark-adapted rabbit retina, Dodt and Elenius[52] found increased sensitivity for blue in the zone of 450 to 490 mμ. In some instances, this was nearly 50% higher than the sensitivity at 500 mμ. Besides, there were slight increases near 600 and 520 mμ. In light adaptation, maximum sensitivity shifted toward shorter wavelengths (in contrast to longer ones in man), the blue peak, at the same time, shifting from 470 to 460 mμ. No Purkinje shift was found. Some increase in sensitivity was also apparent above 550 mμ. These findings make it obvious that there is no photopic dominator in the primarily rod-containing retina of the rabbit, just as none was found, so far, in that of the guinea pig, while the blue modulator seems to be more developed in the former animal than in the latter. The difference between the sensitivity curve described in this paper and the usual visual purple absorption curve indicates that there must be some other photochemical substance present in the rabbit retina besides visual purple, viz., a blue modulator of night vision with maximum sensitivity at 470 mμ and of day vision with maximum at 460 mμ. Much less often, a green modulator, with maximum sensitivity at 520 mμ, also appears. The data are in excellent accord with absorption studies in the guinea pig by Weale. According to this author, indications of increased sensitivity to blue are also to be found in the paracentral and peripheral retinal regions of man.

We must be grateful to Walls[53] for one of the most delightful bibliographic detective stories ever written. Starting from a poorly quoted item in the bibliography of color blindness compiled by Helmholtz almost 100 years ago, Walls set out to find the original publication of one Giros v. Gentilly. This search stretched over several years and led him into all kinds of seemingly blind alleys. From each of these alleys, however, Walls emerged with some interesting and sometimes fascinating information. Finally he was able to find out what Helmholtz actually read (he obviously never saw the original work), what other information led him to what he read, and what the man actually wrote whom Helmholtz did not read. But this is only part of Walls' story. He got (and we get), in the course of his study, acquainted with a great many in-

teresting facts pertaining to many other subjects in addition to color vision: the life history of a fugitive general in a Canadian rebellion; some international scoundrels of that age of Cagliostro; the working of librarians and the *Bibliothèque nationale* of Paris; the history of several long-defunct German scientific magazines and the biographies of their editors, etc. Finally, Walls found out that some obscure man, a chemist probably, whose name might have been George Palmer, but who for some reason assumed the fancy name of Giros v. Gentilly (or vice versa) developed the tricomponent theory of color vision long before Thomas Young and that he had even described what we today call atypical achromatopsia. Helmholtz certainly never became aware of all these facts, and it is mostly owing to his publications that the trichromatic theory received the name Young-Helmholtz. At least part of the credit should have gone to Palmer or v. Gentilly (whichever was his real name).

IV. Refraction, Visual Acuity, Refractive Errors, Optical Aids

In a large sample, of 2000 eyes, Tait [54] found that 1575 had corneal astigmatism between 0.25 and 1.5 D. Only 12 eyes had spherical corneas, and in 29 the astigmatism was 0.12 D. or less. Only in 30 cases was the astigmatism greater than 4.0 D., and in 2 it was greater than 5.0 D. Eighteen cases had irregular corneal astigmatism. The astigmatism was always corrected with concave cylinders; the necessary effective power of the correcting cylinders at 12 mm. from cornea was calculated. Tait publishes a valuable table for such calculations. One finds from this table that, for example, a corneal astigmatism of 4.00 D. is to be corrected with a convex cylinder of 3.25 D. if the spherical refraction is +8.00 and with a concave cylinder of 5.00 D. if the spherical refraction is −8.00 D. Calculations range from −10.00 to +8.00 D. The practically significant values for aphakic correction are unfortunately not included. By extrapolation, however, the practitioner will find that, for example, with a +10.00 D. lens and keratometer astigmatism of 2.00 D. about 0.5 D. less concave cylinder is needed for proper correction. For 3.00 D. astigmatism one needs 0.75 D. less; for 4.00, about 1.00 D. less. From the keratometer readings and the actually found refractive correction, Tait calculated the intraocular (lenticular) astigmatism, and this he found to be mostly of the against the rule variety, with 0.50 D. as its most frequent value in all age groups. Tait advocates the routine use of the keratometer. He notes the usefulness of these data for the differentiation of anisometropias. One group is caused by differences in anteroposterior lengths; another, by unequal refraction. In the latter one will encounter differences in corneal curvature and will expect aniseikonia.

Hobbs and Schimek [55] report on determinations with the Rodenstock refractometer done by one technician on 479 eyes of 242 patients. All these were done without any cycloplegic, independently, and in advance of other methods of refraction. Comparisons were made between refractometer determinations and final manifest refractions on one side and refractometer determinations and final cycloplegic refractions on the other and were expressed in terms of "Rodenstock error" relative to the data of the two other methods taken as standards. Several graphs were drawn to show these "errors" in spherical correction, cylinder power, and cylinder axis. In comparison with cycloplegic determinations, the distribution of these errors followed expected standard deviation curves. The average spherical error was 0.48 D.; the average cylinder error, 0.31 D.; the average axis error, 10 degrees. In comparison with manifest refractions, the standard deviation curves were displaced toward too high plus values, indicating that the accommodation factor played a smaller role in the refractometer determinations made by the technician than in the manifest refractions in the hands of the ophthalmologist. The variations in different age groups were similar.

The magnitude of the error was the same for both myopia and hyperopia. A considerable degree of technical proficiency is necessary to obtain accurate and useful results with the Rodenstock refractometer. Retinoscopy was found a quicker method by the ophthalmologist, and even the skilled technician who performed this study preferred retinoscopy for its greater ease. The authors agree with a former clinical study by Bradford and Lawson on Rodenstock determinations under cycloplegia, that the "use of the Rodenstock Refractometer is not unreasonably difficult or time consuming and gives a reasonable approximation of the refractive status . . . even without the use of cycloplegia."

The duochrome star test of Stepanik [56] consists of a "star" (an astigmatic dial formed by double stripes at angles of 60 degrees to each other) superimposed on a half-red half-green test field. In this manner the advantages of a duochrome test and an astigmatic dial are combined and both the astigmatic and the spherical components of a refractive correction can be refined. The red and green filters transmit the dominant wave lengths of about 650 and 530 mμ, respectively, and their respective foci are 0.4 D. behind and 0.3 D. in front of the retina, assuming (as is usually done) that the retina is accommodated on the yellow part of the spectrum.

In his dealings with deaf-mutes, Miles [57] uses a kind of fingertalk, and he does it in a charming and interesting manner. All the patient has to show is "one finger" or "two fingers." This will indicate his choice between added plus or minus, between the adding or subtracting of cylinder power. It will also give such information as "better on" or "better off." The relationship of Maddox rod and light are represented by index finger and tip of finger. Morrison [58] uses a microphone placed around his own neck and head phones and an amplifier for the deaf patient to facilitate communication during refraction.

Much wisdom is gathered in a short paper by Koch [59] on the manner in which to improve on the procedure of refraction. He recommends a high-power reading addition for the partially sighted and is willing to sacrifice binocular vision to good monocular near vision. He likes to prescribe plastic lenses for errors of higher degrees and always prescribes heat-treated nonbreakable lenses for children.

He is not disinclined to the prescription of oxfords ("they are taken off and put on readily and are easily available hanging on a chain around the patient's neck"). He is in favor of keratometry on every patient. He advocates routine central field studies and scleral tonometry. He likes a well-illuminated examination room. It is interesting to learn that Koch is not an unquestioning partisan of refractive routines ("21 points" or otherwise). "There is nothing sacred about it and should it call for unnecessary testing in a particular case, the routine should be disregarded as it applies to that patient."

It is a pleasure to find another of our optometrist colleagues object to the widespread idea that an examination is only "scientific" if all tests are carried through on all patients. Burman [60] feels that when each patient receives 20 (the sacred number is 21) different types of examination he is regarded merely as a case or an experiment and not as an individuum. Some refractive cases should require 10 minutes, while others may require more than 2 hours. Nothing but the patient's individual problem should decide the length of the examination.

The fruits of years of experience are presented in a small monograph by Bannon [61] on the physiological factors in multifocal corrections. A great amount of information is here collected and tabulated relative to bifocals and trifocals, like the field of view through various segment widths, the calculated interocular distances from infinity to 10 in. (25 cm.) in appropriate steps, the approximate visual acuities when letters of known size are recognized at different viewing distances, the proper reading additions for different reading and working distances, the range of clear vision

through distance lenses and various bifocal and trifocal additions and various amplitudes of accommodation, etc. It is obvious that such a contribution is meant as constant companion and a source of reference rather than a paper to be once perused and many will for many years be grateful for the wealth of information and suggestions collected by the author.

An extremely useful compilation of the visual requirements of railroad workers has been published by Wheelock and Koch.[62] This compilation is based on a circular published by the Medical and Surgical Section of the Association of American Railroads (Circular M&S-300) as revised in December, 1951. One finds in this compilation the visual requirements for entrance to service, for promotion, and for required periodic screening tests. There are three classes (A, B, and C) of jobs, with different requirements, and it should be interesting that, at entrance, even a lampman, a station baggageman, or a track foreman (one of the several job types in Group B) is required to have binocular single vision with no less than 20/40 correctible visual acuity in the poorer eye. For near vision test the Association provides reading cards. It should also be interesting to note that for color vision testing the Holmgren yarn test is still acceptable and that pseudoisochromatic tests are said to be "most accurate when made in daylight." Somewhat strange is the stern but summary disposal of the problem of strabismus ("A person so affected is in the same category as a one-eyed person") and the gloomy view taken of people operated on for cataract ("Post-operative vision, corrected or uncorrected, is usually poor and judgment of distance is impaired"). It is, on the other hand, remarkable how sensible and liberal a standpoint is taken ("In order to prevent undue hardship to an employee in service and recognizing the increased value of such employee because of his experience and familiarity with duties") in the case of reexamination of older employees. Colored glasses are justly forbidden whenever interpretation of colored signals is part of the work of an employee. Sensibly, again, an employee in need of correcting lenses is required to have a spare pair of glasses on his person.

The New York University-Bellevue Medical Center and the Center for Safety Education, New York University, held a joint symposium on the "Medical Aspects of Motor Vehicle Accident Prevention" on May 23, 1956. The Committee on Visual Standards, under the chairmanship of Dr. Conrad Berens,[63] made their report at this meeting, in which they recommended that the usual three categories—of public transportation, interstate commerce, and private car operators—be changed so as to combine the first two into one group. In this group visual acuity is to be correctible to 20/30 in each eye and if glasses are needed an extra pair should be mandatory. Form fields should be 70 degrees in the horizontal meridian in each eye and 140 degrees for the two eyes. "No requirement for color vision indicated. However, it is recommended that the shape, size, position and color of traffic lights be standardized." "No requirement for stereopsis (depth perception) indicated or recommended." "No test for light sense recommended but the presence of night blindness should be excluded by direct question." Yearly reexaminations should be mandatory. In the case of private operators visual acuity should be correctible to 20/40 in the better eye. The form field should encompass 70 degrees in the horizontal meridians in each eye or 140 degrees in the two eyes. Reexamination is recommended every three years.

The Committee also made recommendations to correct the present inequalities of state laws and recommended that consideration be given by designers of vehicles to such factors as windshield wipers, tinted windshields, reflections from chrome, rear windows and mirrors, etc. Several further recommendations were made regarding research on reaction time, muscle balance, and depth perception in their relationship to accidents and for the evaluation of fitness

to continue to drive of those involved in accidents.

An important paper dealing with visual mass screening school programs has been published by Ryan.[64] Especially interesting is his analysis of the data gathered in several experimental screening programs. These were carried out for the purpose of assessing the practicality and the relative efficiencies of the methods used. There are five vision screening procedures which have been widely used in the schools of the United States. Three of them use commercially available instruments; the Massachusetts Vision Test employs a series of clinical procedures but does not necessarily require the use of any commercial device; the fifth procedure is the use of a simple Snellen chart for distance. With all tests, except the last, horizontal and vertical phorias can be measured and the Massachusetts Vision Test also makes specific provisions for the detection of uncorrected nonmanifest hyperopia. The three commercial instruments measure visual acuity both at distance and at near. Some provide for tests of binocular vision, fusion, or stereopsis. All three provide for some form of color-vision test.

One of the most important comparative studies was carried out in St. Louis and revealed that the Massachusetts Vision Test makes an excellent show in respect of correct referrals, which, after all, is the crucial point of all mass vision testing. The Ohio State University study showed that the Snellen test at 20 ft. (6 m.) is the most reliable of all screening procedures if carried out carefully and with proper illumination. Since the Massachusetts Vision Test incorporates this procedure, it can only produce better results than the Snellen chart test in itself. However, the Shrewsbury (Mass.) experimental program indicated that in the lowest grades of school phoria tests are unreliable.

A further analysis of the results of the Danbury study by Leverett[65] showed once more the usefulness of the Massachusetts Vision Test. To assure a high degree of accuracy in this pilot study, all children who once failed were tested a second time and those children already wearing eyeglasses were separately treated statistically. It turned out that of the latter group 58.8% failed at first test and 44.9% on retest, while of the rest of the children 20.4% failed on first testing but only 11.7% the second time. Obviously, those children who need ocular attention and correction perform more poorly even when wearing their corrective glasses. On the other hand, one will expect that of those failing the test in this group a smaller percentage is eventually referred for ocular evaluation unnecessarily.

Some years ago Hirsch[66] suggested a skiascopic procedure for visual screening surveys. During the survey by this method at a group of schools in Los Angeles County, occasionally two records appeared for the same child. The dates of the examinations were no more than one week apart. Thus, inadvertently, an experiment was performed by which the reliability and repeatability of a skiascopic mass screening test could be evaluated. There were 36 such duplicate records discovered among more than 10,000. Hirsch found that in 51 of the 72 eyes of these 36 children the inadvertently repeated examinations showed a difference of 0.25 D. or less and in 14 the difference was between 0.50 and 0.75 D. No greater deviation was encountered. (Standard deviation in this small group was 0.34 D.) In another study on 840 school children measured in the spring and again in the fall, the differences between the two readings gave a standard deviation of 0.36 D. In another study with repeated retinoscopy after six months he found a standard deviation of 0.32 D. Thus, the standard deviation of the accuracy of skiascopy is certainly no less than 0.3 D. and the 90% confidence limit no less than 0.7 D. (This, by the way, Hirsch remarks, throws an interesting sidelight on claims of change of refraction by "training.")

Data of 36 children examined by the same examiner are also interesting. It shows

that the correlation coefficient between the refractive states of the two eyes at the same examination was greater than the correlation coefficient of the identity of two findings on the same eye one week or six months apart. Hirsch correctly recognizes that a certain bias on the part of the examiner toward finding similar refraction on the two eyes cannot be excluded, and he warns that the same bias will prevail whenever a retinoscopic study is expected to prove the efficacy of some kind of therapeutic or orthooptic measure in the treatment of refractive error. (He obviously refers once more to the "treatment" of myopia in so-called vision schools and, alas, by many who claim to be professionals—all still doing blooming business.)

Schwarz [67] measured visual acuity and visual efficiency with colored test objects (Landolt rings). When surround and object had the same hue, visual efficiency was best with yellow test objects. When object and surround were of opposing colors, efficiency was best for red test objects on green background. Recognition of test letters in this setting required both less illumination and shorter exposure time. Visual efficiency was better for light test rings on a dark background than for black test objects on a light test field.

Inouye's test characters for children are known in this country from their inclusion into Berens' textbook. Some of these have now been discarded by their originator [68] and replaced with newer ones, including the picture of an airplane. They also include Inouye's hook (a pattern recommended in the place of Landolt's ring). According to clinical tests, the pictures are recognized by children of 4 to 6 years of age, while 92% of children 5 to 6 years of age recognized the positions of the U-shaped hook. The gradations of the chart follow the old (and antiquated) international standard—0.1 (5/50), 0.2 (5/21), 0.3 (5/17), 0.4 (5/13), 0.5 (5/10), 0.6 (5/8.9), 0.8 (5/6.3), 1.00 (5/5), 1.2 (5/4.2), 1.5 (5/3.3), 2.0 (5/2.5), 4.0 (5/1.25). The latter extremely small pictures are for testing at close range. Inouye suggests that one start at 9 m. distance and come closer if the child cannot recognize 5/5. He makes his approach in the geometric order of 9, 6, 4, 2.7, 1.8, and 1.2 m.—an excellent suggestion. One will agree with the author that small children do not like to be tested from long distances. They should be tested from 1 m. Interestingly, Snellen's original hooks for 5/5 vision were 7.27 mm. in diameter; Landolt's original rings, 7.7 mm. (these were adopted as the international standard in 1909). Landolt's new rings are 6.9 mm. in diameter, and Inouye's is 5 mm., with the thickness of the lines being 1/5 of this value. It seems that what is to be called 1.0 or 5/5 or 20/20 vision changes too.

According to Savell,[69] "Projection charts are to date the most modern means of acuity testing." They certainly make testing easier and save time, especially with such features as the Turville Infinity Balance Test, Worth's four-dot test, duochrome test, Landolt rings, Verhoeff circles, astigmatic fan, etc., incorporated on newer charts.

A projection chart for Japanese patients not familiar with English characters was designed by Corboy [70] on the basis of the Snellen principle. This is quite a problem, since in Japanese ideographic writing variation of the thickness is an essential element. Elementary phonetic characters were therefore used and only slightly modified in order not to lose their identity. By this it was possible to make them conform to the 5 minutes of arc requirement. A simplified astigmatic dial, with a triple line at every 45 degrees, samples of the four standard colors (red, yellow, blue, green), and broken rings for illiterates complete the slide (which is distributed by the American Optical Company).

Measurement of the refraction by Huerkamp [71] on 1065 eyes with retinal detachment, especially of 248 eyes with tear in the region of the ora serrata ("ora-tear"), gave evidence that in these cases corneal astigmatism, unilateral astigmatism, and, especially, astigmatism in an oblique meridian are found twice as frequently

as in healthy eyes. Unilateral astigatism is met with more often in case of ora-tears than in other type of tears. Both, detachment and corneal astigmatism, are, in the author's view, the outcome of a "dysontogenetic" development of the primitive disc and retina. The genesis of myopia is related to this combination of astigmatism and detachment. Unilateral astigmatism was found on the side of detachment with ora-tear in 74% of such cases, while it was present in only 20% on the side of detachment in the case of detachment without tear in that region. In 50 eyes with bilateral ora-tears astigmatism was also bilateral in 82%, while in normal eyes unilateral astigmatism occurs in 32%, bilateral in 68%. Interestingly, in 169 eyes with ora-tear there were only 13% myopes, another 21% having simple or compound myopic astigmatism, while the number of emmetropes was 20%, and 11% and 20% had hyperopia and simple or compound hyperopic astigmatism, respectively. Altogether, 56% of all patients with ora-tear had astigmatism.

The influence of uncorrected errors of refraction (artificially produced in emmetropes by addition of spherical lenses and cylinders in different axes) on visual acuity was analyzed by Prince and Fry [72] under otherwise constant and known surround conditions and pupillary aperture. (Landolt rings were used for this procedure, and the number of correct answers to 60 exposures was registered.) Since the score of correct answers represents some guesses besides the actual correctly seen instances, proper allowance was made for the former and the 50% level of seeing was thus calculated. This magnitude represents, according to the two authors, the only value by which uncorrected visual acuity in refraction error can rationally be expressed. The data attained were of course of only limited clinical value. Since blur circles increase not only with refraction error but also with size of pupil, equal amounts of blur and visual impairment will be the result of different uncorrected metropia under ordinary circumstances. Moreover, artifical hyperopia (induced by minus lenses) is easily overcome by accommodation, thus showing no blur commensurate with the uncorrected error.

An interesting explanation of a long-known phenomenon—night myopia—is offered by Heath.[73] His experiments indicate that at least 1.00 or 1.25 D. of the total amount (usually said to be 1.50 to 1.75 D.) is due to change in accommodation. It is, as this author found, accompanied by another even more significant change in very low illumination, viz., progressive decrease in the amplitude of accommodation, resembling absolute presbyopia. The cause of these, however, is not the low illumination per se (and thus the terms "nocturnal" myopia and presbyopia are inaccurate) but rather the depression of visual acuity which accompanies reduced illumination. Even when sharply outlined targets approach the observer, there is considerable lag of accommodation. ("The observer did not find it necessary to accommodate fully or precisely. . .in order to resolve the smallest letters.") A still greater lag is to be found in eyes viewing blurred targets—the eyes tending to maintain their state of accommodation until the stimulus has changed sufficiently to force a change in the refractive level.

In opposition to Fincham's theory, Heath concludes from these findings that changes in the vergence of light cause only little change of accommodation. When targets are blurred, changes of vergence do hardly change the ocular refraction. Accommodation is "a response to the contrast gradients within the image. . .to obtain and maintain an image with maximum contrast of the details at and near the fixation point. Blurring of the target. . .reduces the gradients of contrast within the image and consequently reduces the stimulus to reflex accommodation."

When a person endowed with binocular vision bifixates an object, it is generally assumed that his visual axes intersect at the point of regard. This, however, has been found not to be precisely the case, as the visual axes might overconverge or under-

converge a small amount and, thus, disparate retinal elements might be stimulated without resulting diplopia. This phenomenon is called fixation disparity. The classic studies on the subject are those of Ogle, who found that appreciable fixation disparity is more probable in subjects with heterophoria and that forced vergence movements influence its magnitude. Forced convergence, e. g., with base-out prisms, increases or elicits a tendency to exophoric fixation disparity. Its clinical study was suggested by several authors as a preliminary test for orthoptic programming and especially as a lead before the prescription of vertically acting prisms. In a study by Arner, Berger, Braverman, and Kaplan,[74] the behavior of fixation disparity under vergence stress was correlated with data of a questionnaire relating to asthenopia symptoms. They found a significant correlation inasmuch as people with no symptoms or patients whose asthenopia symptoms were successfully ameliorated by orthoptic treatment revealed relatively little increase of fixation disparity under vergence stress (added prisms) while those with severe asthenopia showed increase of fixation disparity under the same conditions. This confirms Ogle's data, who also found that people with better fusional ability had lesser changes of fixation disparity under fusional stress.

The authors also studied the statistical relationship between the change of fixation disparity under fusional stress and the scoring of the same subjects relative to the so-called Sheard criterion of visual comfort and found only poor correlation. (As usually stated, the Sheard criterion implies that in order to maintain comfort the fusional reserve must be twice as great as the fusional use or demand.) The question, of course, which the clinical refractionist will want to have answered is left rather open by such a negative result. He will want to know which of the two, the behavior of fixation disparity under fusional stress or the measurements of fusional vergences, is the better of two methods to be used in a practice in which the time for collecting data is limited and to be used judiciously. A statistical study on only 55 cases can hardly be expected to clarify this point.

An interesting case history by Lutz,[75] a psychiatrist, deals with the changing visual acuity of a 7-year-old hyperopic boy. Objective tests verified the existence of a visual acuity of 1.0, while the subjective visual acuity dropped from 0.8 to 0.1 on the basis of a psychogenic visual disturbance. The patient was an "oversensitive, over-timid, normally talented child who had been bullied by his school mates and had reacted with a psychical depression." The visual disturbance arose in direct connection with these insults and disappeared when the depression was successfully cured by psychotherapy.

A paper by Berber[76] supposedly demonstrates the course of visual fatigue "accurately determined in terms of quantitative measures of performance." He used a movable Landolt broken ring both as the measure of visual acuity and as the fatiguing stimulus. The subject viewed the ring monocularly through a 2 mm. artificial pupil and registered the distance at which the gap disappeared or reappeared. Three different retinal illuminations were used. Visual acuity determinations were made for 60 minutes, with a 5-minute rest period following, and then were continued. After 20 further determinations a reading period of 30 minutes was interpolated, and then the whole procedure was repeated. In 17 of 18 such one-hour sessions visual acuity decreased 1.1% to 25.5%, and in 15 of them it recovered completely or incompletely after 5 minutes' rest. It decreased further in the second one-hour session following the rest and the reading than it did in the first one-hour session. Reading had no effect on the already decreased visual acuity in 6 of 12 trials; it increased it in 3 and decreased it in the other 3. Obviously, then, it was not the use of the eyes (as in reading) which decreased visual acuity in the author's experiments but the forced fixation on a gap in a ring and the boredom of such testing. The suggested relationship between the de-

creasing visual acuity caused by fatigue and the increase of myopia in children is certainly very questionable, as is the value of this type of experiment in general.

Myopia caused by prematurity has, according to Birge,[77] several characteristics of its own. It does not progress after its initial occurrence, and it does not fall into the same categories as other more common types of myopia. At first Birge usually corrects one-half of the myopia found by retinoscopy, and in three to six months he increases correction to full. Visual acuity often improves, and in some cases even reduction of correction was indicated. Those not improving usually reveal additional complicating factors, such as brain injury from birth, congenital cerebral deficiency, or nystagmus.

Captain Hynes,[78] of the U. S. Navy, has produced a study of unusual interest of a carefully selected group of healthy young men. These were maintained in an environment, the U. S. Naval Academy, which one will expect to be engineered toward ideal hygiene. Still it was found that the young men who at admission had the required 20/20 vision, but less than 0.5 D. plus spherical equivalent under cycloplegia, developed a myopic type of refractive error. While this refractive error is easily corrected, it interferes with the free selection of, and the assignment to, certain military specialties which require a higher visual efficiency and may disqualify some candidates from being commissioned in the line for which they have been trained. The analysis of the records of several classes repeated the pattern just described in so consistent a manner that, actually, tables of anticipation could readily be constructed to foretell the expected changes. Such tables might turn out to be useful in the selection of candidates for some highly specialized fields. In any event, one will have to be prepared to expect a definite shift from hypermetropia toward emmetropia and myopia between the ages of 17 and 22. The author considers this shift to be in the normal pattern of development, and he does not think it justifiable to indict any influence peculiar to the special environment of the group studied.

In myopic eyes in which there are fundus changes, the anterior section of the eye can be assumed to be almost unchanged. Elongation takes place in the posterior section. Exophthalmometric values should therefore be influenced only slightly. In cases of myopia with no fundus changes any increase in length will be largely anterior and should cause increase of exophthalmometric values. In 22 patients with myopic fundus changes and average myopia of 8.2 D. the difference between the exophthalmometric reading of the less myopic and the more myopic eye was found by Bertelsen [79] to be 0.2 mm. In 14 cases in which there were no myopic fundus changes and the average myopia was 7.0 D. the difference between the less myopic and more myopic eye was 2.3 mm.

The two following papers certainly cannot be left unnoticed. They deal with the correction of a refraction error, progressive myopia, in a manner which is unorthodox and possibly dangerous—by preventive surgery. Neither of them contains detailed description of techniques, complications, or results or sufficient documentation by case reports. One of them gives the most sweeping indications and almost treats removal of a clear lens as a bagatelle. Still, the two papers offer a challenge, and we may not have been doing full justice to patients with this often disastrous condition, if all or even part of the claims laid down in these two papers are valid. More documentation by the authors is urgently needed, as well as unbiased trial by others, at first, at least, on highly selected cases.

According to Barraquer Moner,[80] "in myopes without retinal detachment, the indications of scleral resection are: constriction of visual fields, appearance of scotomas, enlargement of blind spot, diminution of visual acuity, appearance of floating bodies, macular and paramacular hemorrhage, visual disturbances which indicate retinal damage and poor blood circulation. After resection

these phenomena tend to disappear and one gets 'sensible' amelioration of visual field and visual acuity. . . . We aim at impeding the evolution of these lesions with the resection." Barraquer's statistics are based on 205 scleral resections in four years. Of these, 62 were greatly improved, 88 significantly improved, 44 improved, and 5 not improved, and data are missing on 6. On 18 of these cases the Fukala operation was previously carried out; in 13 of them improvement was great; in 5, significant. The clear lens was removed in 90 cases, and in these great improvement occurred in 45 cases, significant improvement in 27, little improvement in 16, and no improvement in 2. The improvement was greater when inflammatory changes were predominant; it was less in cases of atrophic lesions.

The indication for scleral resection is based on the following reasonings: 1. It is a treatment of myopic sclerochorioidosis. 2. It readapts the contents of the globe to its receptacle after lens extraction; it permits the hyaloid to stay in closer contact with the retina and the posterior lens capsule (in case of extracapsular extraction); it diminishes the danger of retinal detachment. 3. It corrects the spherical ametropia and astigmatism by modifying the corneal axes and diameters.

Barraquer-Moner also had some experience with the placing of a retrobulbar "belt," the inclusion of formalinated sclera behind staphylomatous regions, the placement of a band of sclera around the globe from medial to lateral rectus muscle, and the placement of fascia lata around the globe. All these procedures serve, according to him, to reduce the anteroposterior diameter of the eye and reinforce the scleral resection, strengthening the posterior wall of the eye, and work at the same time as a kind of tissue therapy in Filatov's sense. "In no case did we have any operative or postoperative accident." (One case is described in which after retinal detachment in one eye prophylactic scleral resection was done in the other eye. This eye finally developed total detachment in spite of added electrosurgery. But this obviously is not counted as a "postoperative accident.")

In cases of progressive myopia, Friede [81] detaches the iris root in a circumference of 180 degrees. By this method he means to relieve one-half of the anterior ring of attachment of the retina. This should in his opinion, have lessening of tension as a consequence, especially in the region of the macula. Detachment of only one-quarter of the circumference cannot have the same influence on the macular region. Following this surgical detachment, the absorption of aqueous increases and the intraocular pressure falls below 10 mm. Hg. Friede has operated on more than 20 cases in the last 10 years, mostly children under 10 years of age and also some adults. Of these cases, 10 returned for check-ups, and in 8 of them no change in refraction was found. In two cases regression of myopia could be registered (of 3 D. in one of them). The patients received pilocarpine-digitoxin eyedrops and were given calcium and vitamin A and intravenous injections of dextrose.

To make this review somewhat more comprehensive, two communications (one cannot call them "papers") will have to be reported in this place. Their authors chose, of all places, the United Press and daily newspapers to report on their achievements. We thus learn from the *New York World-Telegram and Sun*, Dec. 26, 1956, that Dr. John C. Neill, Department Head at the Pennsylvania State College of Optometry, has been successful in 233 persons in halting progressive myopia with corneal contact lenses, with a follow-up study of four years —a result which certainly merits our utmost attention in case these persons were of the age of, say, 10 to 22 years (which the United Press failed to mention). Of course, every refractionist will have had cases of, say, 22 to 42 years of age, followed for four years or more, whose progressive myopia was "halted" by ordinary lenses, or no lenses at all—and several hundreds of them. Dr. Neill's great discovery might then just be a publicity stunt. On the other hand, if Dr. Neill will deem it not below his dignity to

submit his results to the readers of a scientific magazine, then it will be the duty of serious refractionists to study the influence of contact lenses on myopia, an influence which, after all, is both possible and thinkable.

The other communication, also released through the United Press, under the dateline of Oct. 7, 1956, reported through many daily papers throughout the nation the display at the annual convention of the Illinois Federation of the Blind by Dr. William Feinbloom, a research fellow at Columbia University, of a "new optical lens which, he said, can restore working eyesight to more than half of some 500,000 Americans who are rated legally blind." "The lens is based on a new optical principle of increasing the light-gathering power of the eye" "and allows a patient to achieve a 400% increase in vision, while maintaining a 90-deg. undistorted field of vision." It will be a happy day for ophthalmology, the poor in vision, and the nation when half of this will have been achieved.

A brief report of a case with an unusual complication of diabetes (relative hyperopia following the increase in blood sugar) has been published by Rosen.[82] The patient was a 42-year-old man in whom a myopia of −5.25 and −5.5 D. was reduced to −3.00 D. while he developed diabetes. After the blood sugar became normal, the old myopia returned. Rosen thinks that "the nucleus engages in hydration as well as the cortex of the lens in these cases. This would make the entire lens more uniform in density and there would be less refraction of the ray of light at the zone of discontinuity between the cortex and the nucleus." As another explanation he offers possible weakness of accommodation, but this will be a less likely factor in patients of (or near) presbyopic age.

In the Northern Territory of Australia, where rain is very scarce, the amplitude of accommodation is amazingly low. As Schultz[83] has found, a reading addition of +1.00 D. is common there for a person 40 years of age. Father Flynn, a priest and ophthalmologist at Darwin, has confirmed this experience. Schultz assumes that the high solar infrared radiation is responsible for the premature sclerosing of the lens.

Cataract lenses suffer especially severely from several of the aberrations, especially marginal astigmatism, marginal power error, and chromatic aberration. The latter is corrected by using two different indices of glass in cemented or fused doublet lens form, while for the correction of the first-mentioned errors aspheric grinding is necessary. Modern cataract lenses, studied by Davis and Clotar,[84] combine the two features consisting of a crown glass button or spot placed into the concavity of a flint glass base. The size of this button determines the useful field, the angular size of which is much smaller than the angular size of the lens itself. It is further restricted by the size of the pupil. (The technical details of this study will interest only those who are interested in lens designing.)

Manufacturers have been chary so far of producing toric bifocals with different astigmatic corrections, or different axes in the distance and near sections of the lens. According to Klauber,[85] this offers no technical difficulties whatsoever. While astigmatic bifocals have up to now always been ground with a spherical surface on one side and a toric surface on the other, there is no difficulty in grinding to toric form either the distance or the near section of the first surface, thus securing added cylindric power where such is needed. ("Bitoric" lenses have now for a number of years been produced on special order by the American Optical Company to correct for meridional aniseikonia. This part of the manufacturing skill is therefore not fully new. Grinding as a bitoric one section of a bifocal lens seems to be an entirely new procedure, however.)

A new hard transparent resin, polyallyl diglycol carbonate, possesses, according to Graham[86] (Armorlite Co.), the lightness and great strength of the best previous optical plastics. Its tridimensional cross linked molecular network resembles that of an other organic high polymer, diamond. It

is 10 times more resistant to flying abrasives than methyl methacrylate, the hardest of the earlier transparent plastics. Hot grinding wheel sparks, which ruin a glass lens, do not burn, or adhere to, this resin. This is well demonstrated in the photograph of a glass and a resin lens exposed to welding spatter.

With the use of modern plastic materials available for dentistry and orthopedic and plastic procedures, it is now easy to produce first a negative and then a positive impression of those parts of the face to which eyeglass frames are to be adapted. In certain cases of irregularity of the nose, Dinger [87] finds that such a procedure might have some justification.

According to Cridland,[88] "A British Standard, in any field, is normally a definition of the best in current practice. It is, first, a practicable standard; it is, second, a high standard; it is, third, a desirable standard. It is normally prepared by consolidating the experience of all parties interested. . . . It is, as it were, a hall-mark." The new British Standard of 1956, No. 2738 "Spectacle Lenses," defines the accuracy normally to be expected in points of power, centration, axis setting of cylinder, power and axis of prism, edging, and marking. The back vertex power is used throughout. Tolerances, i. e., limits of permissible departure from a stated measure, are determined. They are commonly set at "one-half of the smallest customary step or interval in the stated measure. Thus, where the quarter-dioptre is the smallest step in general use in prescribing, one-eighth dioptre would usually be the tolerance applied." Since "manufacture becomes rapidly more expensive as precision increases," this certainly is a reasonable standard, though in the U. S., where cost is probably not as much a factor of concern as in Great Britain, manufacturers have set themselves and the American Standard Association suggests much smaller tolerances.

The Ministry of Health of Great Britain has also dealt with a similar problem in the past year and has published its "Report of the Committee on Trial Case Lenses." A summary of this Report has been published by the *British Journal of Ophthalmology*. Like the British Standard, this Report also emphasizes back focal or back vertex power as the most reasonable basis of designating both dispensed and trial case lenses. It deals with the problem of neutralization as a determinant and its serious inaccuracies, the importance of "vertex distance" from the cornea, the history of standards for trial case lenses, the form of trial lenses, and their numbering. Prism diopter is recommended as the unit of trial case prisms. In formulating the standards of accuracy and tolerances, the Committee took notice of the parallel discussions on spectacle lenses which took place in the British Standard Institution, the recommendations of which have just been mentioned. For the laboratory testing of the power of lenses the Committee accepted the wavelength of 5875.6 A., corresponding to the d-line of helium.

American standards for ophthalmic lenses are certainly going to be more rigid. Some of the problems facing the American Standard Association, which has undertaken to set these standards and to make them generally accepted, are discussed by Fry.[89] From his quotations of the standards set for its own use by the Optical Manufacturers Association (April 14, 1954) one sees that tolerances are to be ± 0.006 D. up to 3.00 D. ± 0.12 D. up to 12.75 D., ± 0.18 D. up to 16.75 D., and ± 0.25 D. above this (and one will be wondering if this is good for anything except increasing the cost of lenses). Similar rigid tolerances have been accepted for marked optical centering and thickness, and the power of addition on semifinished multifocals must be within ± 0.09 D. of the marked value. Since semifinished lenses become the wards of the prescription laboratory before being given to patients, whatever high standard is maintained by manufacturers becomes, naturally, only one of the actual standardization problems.

An excellent analysis of some of the still mysterious attributes of Sturm's conoid by

Askovitz [90] clarifies the optical characteristics of the clinically significant circle of least confusion. It is not, as is often assumed, halfway between its two focal lines. Moreover, its area is not (as, again, is often assumed) the smallest. Halfway between the focal lines the conoid has an elliptic cross section, and the area of this cross section is not a minimum but a maximum. The circle of least confusion is always nearer the first focal line, and it divides the interfocal interval into two sections which are proportional to the focal lengths of the astigmatic system.

In publishing a full-length, if elementary, essay on the effects and the uses of prisms, Franceschetti's [91] main purpose seems to have been to show the usefulness of a nomograph method published by the late T. D. Allen in 1939 for the computation of a resultant prism at oblique axes in case prescription of horizontal and vertical prisms is indicated. (On Allen's chart the axis values are marked from 0 to 360 degrees and run counterclockwise, as if the physician were facing the patient. No transposition is therefore necessary.) Since the subject seems to be little-known in the French-speaking part of the world and even looked upon with some apprehension, he found it necessary to discuss the optical effects of prisms and the different prismatic units used in clinical practice as an introduction. This is followed by a lucid explanation of the prismatic effects of lens decentration in the case of both spherical and cylindric corrections. (The name of Prentice is not mentioned.) Most interesting for American readers are some of Franceschetti's remarks regarding the indications for prescribing prisms. He asserts that in convergence insufficiency orthoptics are indicated, but he feels that presbyopes with exophoria for near benefit from base-in prisms. He advocates the prismatic correction of even small vertical phorias. He prescribes partial prismatic correction for acute concomitant strabismus and also for paralytic strabismus. Divergence insufficiency he finds less rare than is generally assumed, and he finds the results of prismatic correction in this condition often extremely successful.

A survey by Tait [92] on optical aids in severe visual disability offers a welcome source of information on all types of optical aids with easily understandable diagrams. He gives all the necessary specifications for the grinding of the Tait telescope, together with data on several doublet magnifiers which, using this information, any well-equipped optical shop should be able to grind. There has lately been some publicity about aspherical compound magnifiers. Tait does not think too highly of them.

The term "magnification" has, according to Linksz,[93] a different meaning in geometric and in practical ophthalmic optics. In the former it means the relationship image size-object size; in the latter, it refers to the spreading of the retinal image by some optical device upon a larger number of retinal elements. If it enlarges the diameter of a retinal image by two, a device is said to have 2× magnification. The simplest method of spreading the retinal image is by bringing objects closer. If an object cannot be brought closer to the eye (for example, if one studies the sky or wants to see a stage production), telescopic magnification is indicated; if it can be brought closer, then the eye has to overcome the large negative vergence of the object rays. This it can accomplish either by accommodation or by borrowing plus lens power. Telescopic lenses have rather limited use as aids for the partially sighted. Of the near vision aids the simplest is the magnifying hand loupe. For the advantageous use of this, the author develops a few simple rules and also gives several practical examples. With the help of other examples, he explains the use of stronger than usual reading additions, of the so-called "microscopic" lenses. With several additional examples he develops some rules by which one can choose the reading addition of proper strength for any specified reading task with the residual visual acuity available in individual cases.

The most comprehensive review to date on the subject of visual aids is that of Kestenbaum and Sturman.[94] These authors divide the reading devices into (*a*) magnifying eyeglasses, (*b*) magnifying lenses or loupes, and (*c*) telescopic loupes. Among the magnifying eyeglasses, they pay special attention to one group of them, the so-called microlenses. (The uninitiated reader will not readily see the difference between magnifying "eyeglasses" and magnifying "lenses" and will not easily understand why some of them are called "microlenses."* The development of some common and more descriptive nomenclature is certainly indicated.) The authors' experience was that magnifying eyeglasses are the ones most suited to help in cases where high magnification is in order. Since very strong plus-lenses (lenses up to +40 to +50 D. have been in use lately, and Dr. Volk, of Detroit, has been grinding lenses of 100 D.), weight and aberrations become quite a problem, and one way to cut down on both of them is to reduce their diameter. (This makes a +50 D. lens a "microlens" of 12 mm. diameter.) An exceedingly interesting and valuable section of this long paper is the one called "Near Vision vs. Far Vision." In this the authors discuss those conditions in which near vision and far vision are unequal, and they succeed remarkably in clarifying the often little-understood reasons for these differences.

Fonda[95] found that a great number of patients with low vision (240 out of 500) could be partially rehabilitated with special lenses. On reexamination, 77% of these patients found the lenses useful and used them. There seemed to be little need for telescopic spctacles, especially for distance use. One possible field for their usefulness would be the television screen. However, most patients prefer to sit close to the set and obtain magnification by approach. In 10 cases telescopic reading lenses were replaced by other magnifying devices and were found preferable. Only one patient, a shoemaker with high myopia, preferred telescopic lenses for work, since they gave him the needed distance to carry out his trade. Otherwise, even for near vision, several of Fonda's patients found bifocals with strong reading addition or simple strong plus-lenses or doublet magnifiers preferable to a telescopic lens with a reading cap.

In many cases it was just a regular, good refraction which helped. Many patients with high myopia, aphakia, etc., are not wearing glasses at all or not the proper glasses and are greatly helped by simple lenses. In all, 138 patients were given strong reading additions of 8.00 to 36.00 D., many in bifocal form. Doublets (Feinbloom type of lenses) were given to 31 patients, their magnification ranging from 8 × to 20 ×. The best results were achieved with the 8 × and the 12 × lenses. Hasting's triplets with 10 × to 14 × magnification were given to seven patients. Contact lenses were prescribed in seven cases, and results were good in five of them. These were cases in which there was corneal pathology or high myopia.

Sloan and Habel[96] also believe that optical aids should be selected with the minimal amount of trial and error. The procedure necessary to find the optical aid best suited for each individual case may be divided into three steps. One decides first of all what amount of magnification of retinal image is desired or necessary. Then one determines the closest distance, expressed in diopters, at which the patient can sustain accommodation for reading, and, third, one finds the smallest size print the patient can read at 40 cm. This measurement determines the factor by which the retinal image must be increased to permit the reading of, say, ordinary newsprint. The authors consider, separately, the magnifiers in which the distance from object to lens can be varied and those in which it is fixed and also the new projection magnifiers, in which the observer views not the enlarged virtual image but an enlarged real image formed on a screen.

* The term microlens has lately also been attached to a type of small corneal contact lens.

Small so-called microscopic magnifiers (which look much like bifocals) of 2×, 4×, 6×, 8×, and 10× power (some of them having diameters as calculated by Kestenbaum) were introduced by the American Optical Company and are described by Carlsen.[97] Lenticular lenses of 4×, 6×, and 8× power with aspheric curvatures which "permit larger magnification with minimum sacrifice of field and definition" under the "I-Gard" trade name have also been announced. Also, telescopic spectacle loupes with 2× and 3× powers have been introduced by "Armco." The clinical usefulness of the first set seems assured, according to results published by Fonda and Kestenbaum; on the latter two sets information is restricted to the manufacturers' statements. An impressive exhibit by Keeler, of London, at the 1956 meeting of the American Academy of Ophthalmology and Otolaryngology of all kinds of visual aids for distance and near vision is worthy of mention.

It is fitting that the centennary of von Seidel's work brought two important contributions to the problem of actual image formation, the aberration, so to speak, from the ideal point-to-point imagery assumed to occur in the kind of elementary geometric optics which is the only one familiar to the average ophthalmologist. Mlle. Flamant has produced a new and thorough analysis of the distribution of light in the retinal image, and Emsley,[98] a distinguished teacher of optics in Great Britain, has added another volume to the standard texts on optics for which he is justly famous, a book on "Aberrations of Thin Lenses." Flamant's[99] work is fully outside the reach or interest of anyone but a specialist, though published in a magazine of primarily clinical interests. Emsley's book will also not interest others but those dealing with lens designing, but no more than the average college training is necessary to understand its mathematics.

The Royal Air Force of England has been finding amblyopia ex anopsia a problem because of the added vulnerability of those so affected should they sustain injury to, or infection in, the better eye. Catford[100] made a comparative study of the distance and near vision of 50 applicants to the R. A. F., with distance vision of 6/60 in the amblyopic eye, or worse, and found that 54% of them had "reasonable" near vision ("N12 or better"). The percentage was even better in the case of myopes with amblyopia. Such evaluation before admission will be important. The study was done with a neat little instrument, the R. A. F. Near-Point Rule, devised by Air Vice-Marshal Neely,[101] a metal slide of 50 cm. length which carries on a rotatable quadrilateral (1) reduced Snellen test type, (2) Times Roman type face, (3) a reproduction of a section of the telephone directory, and (4) a vertical line and dot for convergence measure.

The study of vision with a stabilized image constitutes one of the most exciting new methods of investigation into the working of the visual apparatus. In the simplest of devices for this study, a retinal image is produced by a stimulus pattern carried by a stalk which itself is attached to a contact lens placed on the eye. By this method the image pattern can be kept stable on the retina in spite of the unavoidable constant movements of the eye. It turns out that under this arrangement the seen pattern fades out and even disappears in one to five seconds and then the field itself blacks or browns out. After about 10 seconds the eye makes a sharp and uncontrollable movement and the whole circle of seeing and fading starts again.

A good survey of the work carried out on this subject has been given by Ditchburn,[102] one of the main contributors to our knowledge of this particular problem. As he writes: "It is difficult to convey to a person who has never seen it, the strange quality of vision in the absence of eye movements. The 'information' reaching the brain from the retina is of a kind never before experienced." The effects of the stabilization of image could be neutralized by producing artificial displacements of the seen pattern. Vibrations of 0.25 minutes of arc at 20 cps or individual flicks of 2

minutes excursion were sufficient. The stabilization was found to affect the discrimination of hue, saturation, and brightness. Experiments with a stabilized retinal image so small that about 70% of the light falls on one cone, speak against the color vision theories according to which three different types of cones would be needed for the appreciation of the normal variety of colors. "The results so far obtained show that eye movements are essential to normal vision."

If the minimum angular distance at which two points are just visible separately can be deduced from an involuntary physical reaction, one speaks of "objective" determination of visual acuity. Professor Goldmann of Berne has been advocating the study of optokinetic nystagmus for this purpose, using as stimulus a checkered stripe which moves to and fro in front of the eyes, on a uniform background. This moving checkered pattern can only cause nystagmus if the individual squares are separately visible; otherwise it does not stand out and its oscillations cause no nystagmus. In the instrument described by Schmidt,[103] the frequency of the oscillating movement is 40 per minute. The width of the individual squares is 1.15 mm., and their characteristic pattern, when at rest, should be visible from a distance of 3.80 m. It was found that in persons with 1.0 vision optokinetic nystagmus stopped when the pattern was moved at the distance of 1.6 to 1.8 m. Thus, this distance corresponds to 1.0 visual acuity. The method can be employed even if visual acuity is as low as 0.1. Differences between "subjective" visual acuity and "objective" visual acuity as determined in this test were found not to exceed 20%.

An extremely simple, easily understandable discussion of the optics of contact lenses is offered by Swaine.[104] His calculations can be followed by anyone understanding the most elementary algebraic symbolism and familiar with such basic optical terms as vertex power or effectivity. Even if one leaves all calculations to the manufacturer, it will be of interest to learn that in one system of correction by contact lens the lens itself is afocal, so that the change of refraction is caused by the liquid lens between contact glass and cornea, while in another type part of the correction is incorporated into the lens itself.

V. Clinically Useful Optical Methods

Rotter,[105] an associate of Hruby's in Vienna, discusses the technique of the biomicroscopy of the posterior eye. He gives detailed instructions for successful examination. The contact lens with plano front surface nullifies the refractive power of the corneal surface and makes the interior of the eye accessible to study by slit illumination and corneal microscope. The pre-set concave Hruby lens is best suited for general clinical application. In highly myopic eyes a convex lens should be used for the visualization of the periphery. The Goldmann lens with its three mirrors is also excellent. The stereoscopic accessibility of fundus details depends on the location of the slit image within the stereoscopic field, and this is determined by the angle of convergence of the binocular microscope objectives. Both this angle and the angle of incidence of the illumination must be small to permit stereoscopic observation of eyeground details. This, on the other hand, restricts the stereoscopic field. Central illumination (as presented by the Zeiss instrument) is held to be disadvantageous. Since all three paths, that of the entering illumination and those of the emerging useful monocular bundles, have to pass the pupil, the limited pupillary area is better exploited if the illumination slit is horizontal and the emerging light paths are above or below the latter. The Haag-Streit slit-lamp needs an added prism set to make horizontal illumination possible. When a convex lens is used, one has to deal with an inverse image and the distance between the observer's and the patient's eye has to be increased by about 4.5 cm. This, to be sure, adds another problem, as slit-lamps with a "joy-stick" system may not have sufficient mobility. The centering of the pre-set lens is well taken care of in the

Zeiss instrument. This instrument also provides for a constant distance between eye and lens. However, this advantage is partially offset by the lack of adjustability of distance.

The use of the Schepens-AO binocular indirect ophthalmoscope is described, and several excellent suggestions as to details of the examination are made, by Brockhurst.[106] He does not mind telling us how to hold the intercepting lens, where to stand, where and how to place the chart on which fundus details are to be indicated, how to use the scleral depression properly, how to dilate the pupil, and how to steady the patient's eye by fixation—all useful information which it otherwise takes long experience and much aggravation to accumulate.

For viewing the fundus during removal of intraocular foreign bodies, Dixon [107] reviewed a more than 100-year-old method of Coccius. He placed a glass microscopic slide, with one end tapered to half its normal width, over the cornea with a drop of saline. The fluid fills the space between glass surface and cornea and neutralizes its optical power. The interior of the eye thus becomes visible when one simply looks through the slide. For illumination, Dixon uses his own instrument or the Schepens-AO binocular ophthalmoscope.

A stereoscopic operating microscope with illuminating system offers, according to Becker,[108] attractive possibilities in ophthalmic surgery. The Zeiss operating microscope was for this purpose simplified by Dekking.[109] He uses leg and knee to adjust the instrument, thus keeping his hands free. He has found that the head of the patient needs to be fixed before the operation, as under the given (unusually large) magnifications the usual precautionary arrangements are insufficient.

Another paper, by Barraquer [110] (Bogota, Columbia) deals with the same subject. He too recognizes the difficulties arising from great magnification and "false projection" which are controlled with practice only. However, by the pedal attachment he finds it possible to maintain correct focus while both of his hands remain free. Adaptation of the slit lamp to the operating microscope makes it possible to regulate the intensity of the light and combines the advantages of lateral illumination and optical section with those of axial illumination. Adding a 10 D. concave lens to the optical system, Barraquer increased the focusing distance to 15 cm., which is a further improvement. The focus of the slit lamp and the microscope can be adjusted to the same plane, and the pedal attachment will change both in the same sense.

Goodside [111] emphasizes the significance of a rather neglected diagnostic examination. He feels that the knowledge of the retinal reflexes and their variations allows the observer to spot otherwise readily overlooked pathological processes.

López-Henriquez [112] presents a procedure for direct ophthalmoscopy and retinal photography by which disturbing reflexes are eliminated. This is achieved by inclining the mirror by which the light from a source is reflected into the eye. In this arrangement the mirror itself serves as a screen for the reflex and the observing eye or the camera receive reflex-free images.

The principle of the direct ophthalmoscope is used in a small hand fundus camera constructed by Noyori.[113] This instrument is built in the manner of an electric hand ophthalmoscope; it carries an especially made small flash bulb and an attached camera.

With a concentrated, powerful light, Meyer-Schwickerath [114] has succeeded in producing photocoagulations of the fundus without opening of the eyeball. The instrument used for the purpose is essentially an ophthalmoscope. It is supplied with a special type of lamp which at first can be used for the usual fundus study. After this is accomplished, the intensity of the light can be sufficiently increased to burn the retina and produce an adhesive scar. The instrument can also be used (with some slight modification) to produce an artificial pupil of the iris.

A new instrument designed by Pristley and Foree [115] serves for the study of Scheerer's phenomenon, the entoptic perception of one's own blood cells circulating in the perimacular capillaries, arterioles, and venules. The authors found that not all persons are able to report whether the movement is jerky or uniform but that all are able to estimate the number of moving light dots. Normally, 20 to 25 cells are reported with pulsating motion. No cells, or fewer cells in one eye than in the other, or a decreased number in one sector of the field are abnormal responses.

According to François and Verriest,[116,117] scotopic campimetry merits clinical use. It reveals changes which photopic perimetry does not usually show, especially in affections connected with hemeralopia and in macular affections. In vascular retinal disease scotopic visual fields are also often and early affected, even if the photopic visual field is still normal. In hypertensive retinopathy, retinal edema produces pericecal dark scotomas. In central serous chorioretinitis, a pericentral or pericecal scotoma can be found even if one is absent in photopic campimetry. An imminent thrombosis will often cause a pericecal dark scotoma or enlargement of the central scotoma which is normally present in the dark. In papilledema, differential diagnosis of pseudomeningitis is possible. (The technique used was first introduced by Livingston. It deserves wider application.)

Hylkema's [118] projection perimeter consists of a globe segment illuminated to 250 lux. The movable test light provides twice this illumination, and it can be projected all over the illuminated surface. The size of the test patch can be varied from ½ to 4 degrees. Colored and neutral filters permit the determination of various discrimination thresholds. The instrument can also be used to determine CFF on any part of the retina, since it is equipped with a sectored disc and a motor capable of producing intermissions of 10 to 77 per second.

Harrington and Flocks have already noted the poor performance of aphakic patients with their field screening test. They attribute this to optical factors associated with the high power of aphakic corrections. Strong convex lenses are undoubtedly partly responsible for the apparent constriction of the visual field. Besides, aphakic cases, when looking through their distance correction into the Harrington-Flocks screening device, are undercorrected by about 3 D. Peripheral aberrations can also be blamed for some of the reduction in the visibility of test targets whenever these are at some distance from the optic axis of the lens. The actual location of the targets in the test under discussion is 20 or 25 degrees from the optic axis. (The prismatic power inherent in the strong convex lenses worn by these patients causes an even greater apparent outward displacement.) However, these factors cannot explain the field defects of aphakic patients regularly encountered in the test, and, in fact, these defects are more marked than those found on the conventional tangent screen with the same eyeglasses in the same cases. The special feature of the Harrington-Flocks test is the ultraviolet light reflected from the white test card with maximum emission at 365 mμ. At this wavelength the sensitivity of the lensless eye is almost 1000 times greater than that of normal eye. The ultraviolet light reflected from the white background will therefore be seen as blue by the aphakic, and this will greatly reduce the visibility of the patterns, reducing both their color and brightness contrast. Sloan [119] performed the test, therefore, with a modification. She reduced the visibility of ultraviolet light by interposing a Wratten filter which absorbs all radiation below 400 mμ between the test and the eye. In 10 aphakic eyes she found marked improvement in performance by this method, while repetition of the test without filter resulted in the expected poor performance. (By the way, she found that reduction of general illumination of the test plates to 1.9 ft-c. from the 6 ft-c. advocated by the originators of the test increased the efficiency of the test even in normals.)

The main purpose of a new set of test cards by O'Brien [120] is the quick detection

of visual field defects, especially of central scotomas. It is not meant to supplant perimetry as such. The set is to be used with a hand stereoscope. Simultaneous macular perception is a prerequisite for the successful application of the test.

An ingenious fluorescent lighting system to illuminate the tangent screen has been invented by Berk.[121] In this system red, green, or blue filters can be rotated in front of a white fluorescent bulb, and so, in case one wants to study the visual fields for different colors as well as for white, the same white test objects can be used throughout, the color of the test object being changed by interposition of the desired filter. The intensity of the white or colored lights is easily determined, whereas to measure the light reflected for a small colored test object is almost impossible. The illuminating system provides for about 10 ft-c. of fairly uniform illumination when the white light is used.

Washer,[122,123] of the National Bureau of Standards staff, has designed a spectacle lens tester to measure the marginal power of a spectacle lens with accuracy. The essential principles of this instrument have now been utilized by him to design a marginal power attachment to be used with any commercially available vertex power instrument. A description of this instrument has also been published by Lorant.[124]

A direct-writing electroencephalograph was modified by J. ten Doesschate [125] so as to make nystagmographic recordings.

Simple auxiliary lenses and tubes recommended by Prince [126] as additions to the retinal camera provide for an increase of magnification by 2× and more. In fact, the optic nerve can be made to cover most of a 35 mm. frame without noticeable reduction in resolution.

An interesting practical point is raised by Haynes [127] in connection with the use of occluders. He feels that the often-used translucent occluder over the dominant eye produces a veiling glare rather than forces suppression of the visual impressions conveyed by the occluded eye. Opaque occluders are his choice.

VI. Binocular Vision, Space Perception, Aniseikonia

The most important contribution of the year, in my opinion, to the study of space perception comes from the pen of Rønne.[128] (A long excerpt of this study appeared in the *Survey of Ophthalmology*, with running commentary by me.) Rønne makes five basic assumptions. He believes (1) that there exists a point-to-point relationship between retinal functional units and their respective end-stations in the occipital cortex; (2) that individual ganglion cells which in the visual cortex represent the end-station of the visual pathway from a certain locus of one retina are physiologically coupled with corresponding individual ganglion cells which similarly represent a certain locus in the other retina; (3) that so-called retinal correspondence is the representation and the consequence of this cortical correspondence; (4) that correspondence is innate, "anatomically preformed"; (5) that potential couplings exist between disparate ganglion cells, and, finally, (6) that the physiologic significance of these couplings is to be found in the establishment of a surface of reference in relation to which (in front of it or behind it) all other points in subjective space are localized.

During alcohol intoxication retinal rivalry is absent and sensory fusion and stereopsis are inhibited (Bárány and Halldén). This demonstrates that "integration and suppression are virtually complementary expressions of one and the same basic process."

Normal binocular vision (fusion and stereopsis) depend, according to Rønne, on integrative processes in the occipital cortex. The basis of this integration is to be found in the anatomical and physiological peculiarities of the substratum (the "couplings"). Visual space is characterized by the presence in it of a surface of reference (Hering called it the *Kernfläche*). This surface of reference is determined by the innate "anatomophysiological" coupling of pairs of

ganglion cells in the visual center. Correspondence of retinal elements is just another way to refer to this coupling. It is not a rigid one, since functional coupling of others than the actually corresponding cells is potentially possible. This latter kind of coupling results in the perception of depth in relation to the surface of reference. For coupling to be effective, identity of impact in the two monocular layers of ganglion cells is necessary and disparity, if it exists, must be below a certain limit. If the disparity limit is passed, an appropriate motor impulse will tend to diminish the disparity. This, of course, changes the surface of reference. Retinal rivalry is a prerequisite for the successful binocular integration of disparate stimuli. The assumption that suppression or replacement of one of the paired stimuli plays a dominant role during the normal physiological conditions of vision is not in accordance with observed facts.

A no less significant, though popularly presented publication by Sperry [129] also confirms the old Heringian view about the innate character of space perception—if only in the lowest vertebrates. Matthey and Stone cut the optic nerve of adult newts and found that in time they recovered their vision. New nerve fibers sprouted from the cut stump of the nerve and managed to grow back to the visual center. Fish, frogs, and toads (but not mammals) could also regenerate an optic nerve and recover vision if the nerve was cut without damage to the main artery to the retina. Matthey found that the regenerating fibers wound back toward the brain in a hopelessly mixed-up condition. Still, order was restored. The first possible explanation for this was "learning." The second was some "affinity" between individual fibers and optic lobe cells by which a fiber manages to get back to its proper place. Sperry in one set of experiments reversed the eyes of newts without cutting the nerve. The animals revealed reversed vision and never, during two years, learned to see normally. Reinversion resulted in immediate "normalcy." In another set of experiments, in which he cut the optic nerve, an organized pattern of vision regenerated in every case. Evidently, the individual nerve fibers from the retina, after regeneration, all regained their original relative spatial functions in projecting the picture to the brain. Reversed vision is more disadvantageous than no vision at all; still, the animals were unable to do anything to correct it. Learning did not help. Orderly recovery was not achieved through function and experience, through learning, but rather was predetermined in the growth process itself. In some of the animals, Sperry destroyed small parts of the optic lobe after nerve fiber regeneration and found blind spots in corresponding parts of the visual field. Any ingrowing fiber seems thus to attach itself only to the particular brain cells which match its individual chemical flavor. The regenerating fibers apply a shotgun approach. Each fiber puts forth many branches, and the brain cells, too, have many branches. However, the great majority of contacts come to nothing, until eventually one of the growing branches encounters a type of cell surface for which it has specific chemical affinity and to which it adheres. The theory of inherent chemical affinities among nerve fibers and cells is, according to Sperry, better able to account for the behavior found in the experimental animals than any hypothetical mechanism based on experience and learning.

The necessary conclusions from this fundamental work are that the sense of direction and of location in space, the sense of position of the visual field as a whole, and the perception of motion are built into the organism and do not need to be learned.

Hess [130] manipulated the sight of newborn chicks with tiny hoods to determine whether their ability to locate objects is learned or innate and due to a process of maturation. These hoods held experimental goggles over the eyes of the chicks, leaving the beak free for pecking and eating. In one experiment prisms fitted into the goggles caused the chicks to see everything 7 degrees to one side of its actual position. If localization of

objects in space could be learned, performance should be unaffected by this fact. However, the chicks did not peck in some random fashion until after trial and error they "learned" to find the objects to be eaten. They pecked with increasing ("learned") accuracy, but always 7 degrees to one side of their target. Chicks kept for days in this condition were underdeveloped owing to starvation; two of them actually died after a week. Hess concludes that the chicks' visual apparatus for locating objects is innate and not learned. They did not simply peck at random until hitting the target, and they were unable to learn through experience to correct their aim. A similar technique was used by Hess in experiments to study stereopsis in adult chickens. He fitted base-out prisms over both of their eyes (in man such prisms make things appear closer than they actually are). All six animals used in this experiment pecked short of the grains or meals placed in front of them. None struck the surface on which the grain rested. When one eye was covered the hens pecked to the side away from their exposed eye. "The conclusion to be drawn is that the normal adult chicken uses binocular cues to localize objects in space." The same, however, was true with newly hatched chicks without visual experience and with adult hens which from birth were prevented from using binocular cues.

"To what extent changes in convergence might contribute to stereoscopic acuity" is the subject of a paper by Ogle.[131] The more recent discovery of muscle spindles in the extraocular muscles of man and certain animals has once more enlivened the discussion about the proprioceptive sense from these muscles (so eloquently advocated by the late Chavasse). Wright found that stereoscopic acuity improves measurably if under experimental conditions eye movements are permitted. However, Ogle's interpretation of these results suggests that eye movements play little or no role in this improvement. The stereoscopic threshold of depth perception is, according to Ogle, a function of peripheral visual acuity. The ability to discriminate differences in disparity depends on the resolving power of the percipient elements in those parts of the retinas on which this discrimination rests. Whenever the eyes fixate some point A, the images of another nearer or farther point B fall on slightly disparate, peripheral retinal points with poorer resolving power. However, when the eyes are permitted to look from A to B, and back, then, while the eyes move, both eyes are continuously stimulated by both points. Thus, on the average, the images of both A and B fall on retinal regions with higher visual acuity than the disparate images of B would fall on while A is fixated. When the eyes look at a point halfway between A and B, stereoscopic acuity is maximal.

The sense of depth cannot come from a convergence change, according to Ogle, because the disparity thresholds are so far below the threshold for the muscle sense. This does not exclude, however, the existence of feedback innervations useful in executing accurate fixation eye movements. That this statement by Ogle will also not be accepted as the last word should be expected. In fact, Ishak, Hefzalla, and Badawy[132] once more repeated Wright's experiments, adding some further modifications and (in their note to the editor of Ogle's paper) again came to the conclusion that "convergence has a role in stereoscopic vision," a conclusion with which Ogle[133] (in his reply to this note) could not fully concur.

The just-discernible difference in depth is, according to Westheimer,[134] a function of (*a*) interocular distance, (*b*) threshold difference in binocular parallax, and (*c*) observation distance. Magnifyers and prisms change the acuity of depth resolution, since their use makes the threshold further dependent on the optical properties of these devices and their distance from the eyes. The exploitation of the optical advantages they might offer is restricted, however, since they must permit the formation of clear retinal images, simultaneously, on the foveas of both eyes. Plus lenses and base-in prisms within the just-defined limits

enhance depth resolution. In tasks demanding high resolution at close observation distances, for example in ophthalmic surgery, magnification devices consisting of plus-lenses and base-in prisms will therefore be found advantageous.

Starting from some simple observations of clinical practice, Colenbrander [135] concludes that the eyes have two ways of localizing direction: (1) binocularly, or in a coordinated manner, and (2) monocularly, or independently. To this comes haptic localization, e. g., by the hand. When these contradict each other, either localization becomes double, or one organ dominates and blocks the other organs, or, finally, there may be a compromise. This, in his opinion, explains the development of abnormal correspondence in which the relationships between the two eyes are abolished and localization by the squinting eye becomes independent. The term "false projection" is incorrect. Strabismal patients with normal correspondence localize falsely; those with "harmonic anomalous correspondence," correctly.

The old question of why the architrave of the Parthenon is not straight and still is being seen as straight has been answered by Colenbrander [136] once more. He believes that the solution is to be found in the appearance of angles which we all have the tendency to see more right than they actually are (see the distorted rooms of Ames as a modern example). Since the slanting sides of the tympanon form acute angles with the architrave, the latter would appear sagging if actually straight and had to be made slightly upward curving to appear straight. As a proof for his explanation Colenbrander reminds one of the Madeleine and the Chambre des Députés in Paris, where everything is straight but the architraves appear sagging. These buildings impress our author as lifeless, while "the unprejudiced knowledge of the human mind which is so clearly shown in this majestic building [the Parthenon], is awe-inspiring."

Studies on the stereoscopic vision of normal children between the ages of 6 and 11 years were carried out by Sachsenweger and Junker [137] with the well-known falling beads of Hering and with a modification by Best of the classic three-rod horopter instrument. With the first method, children performed as well as adults, once stereoscopic vision was present at all. With the latter instrument, the authors found a close correlation between performance and age up to the age of about 9 years. After this, children performed as well as adults. There was no correlation with pupillary distance or degree of intelligence (school marks), though youngsters with good power of concentration and attention (the classification was made by the teacher) scored better. The authors conclude that the falling beads test can be used with confidence to determine the existence or nonexistence of stereoscopic vision in early childhood.

Sachsenweger,[138] in a new study of Panum's areas, confirmed the well-known fact that these areas increase toward the retinal periphery, while the "stereoscopic space" decreases in thickness. This space is greater in front of the horopter (served by crossed disparity) than behind the horopter (served by uncrossed disparity). The two "spaces" (the space of fusional or Panum vision and that of stereopsis) do not change in a similar sense; consequently, in the periphery it is possible to have fusion with images falling on horizontally disparate retinal points while, at the same time, no stereoscopic localization results. When stimulus time is reduced, stereoscopic space becomes narrower, but Panum's areas increase in width at the same time. In a similar manner, lowered illumination diminishes the faculty of stereopsis, while Panum areas again become larger. The same is true in fatigue or when visual acuity is artificially reduced by convex lenses. Experience has the opposite effect. Sachsenweger thinks that this proves that "Panum vision" and "stereoscopic vision" are different sensory achievements (*Sinnesleistungen*). He thinks this fact to be of some interest to orthoptics, as many still assume that simultaneous vision is identical with stereoscopic vision.

Brückner [139] found that a stereoscopic effect is recognizable even in afterimages; however, only gross depth difference could be distinguished and finer stereoscopic details were lost—just as fine details are altogether not recognizable in the usual afterimage. The main reasons for all this, Brückner thought, were impossibility of sharp fixation for the 30 seconds or more which are needed to impress a sufficiently lasting afterimage and the impossibility of scanning, by which different aspects of a stereogram are under ordinary circumstances brought into the range of central vision. Looking at any pattern to produce an afterimage of it, one cannot help fixating on one detail only, while all other details, especially those more peripherally located, necessarily appear in physiologic diplopia. Their finer depth differences will, thus, be lost.

Previously reported observations, especially by Verhoeff, according to which the stereoscopic perception of disparities in static line configurations was reduced whenever the image of one eye was darkened, have been reexamined by Ogle and Groch.[140] They used three different experimental arrangements in which they could measure the amount of the reduction of stereoscopic acuity if such indeed occurred. Their experiments could not verify the original observations. They therefore conclude that the disparity of retinal images maintains its integrity even though the luminance of one of the two stimulus patterns might be markedly decreased. This conclusion is, of course, only true for static configurations and has no bearing on the well known Pulfrich effect. As to the Verhoeff effect, the existence of which is not corroborated by these studies, the authors refer to the dangers of "making too sweeping a conclusion from introspective observations made from figures drawn to be seen in a stereoscope."

Morrison [141] has devised a convenient instrument to produce crossed or uncrossed double images of a light within 20 ft. (6 m.) and on both sides of a fixated light. Polaroid filters and a short exposure time (0.66 second) were used. Only a small number of subjects were tested, and only one did correctly judge the relative position of the disparate stimuli as being in front of or in back of the fixation light in all of 10 exposures. Another subject gave 8 correct answers out of 20 settings (which, incidentally, is less than chance), and another subject's score was 11 out of 20. When the disparity exceeded what Ogle calls the zone of binocular vision, the first observer could still give 7 correct replies out of 10 settings, although she saw double—two lights in front of or in back of the fixation light. The author admits that it is hard to conceive how pure sensory stereopsis could occur under the conditions of his experiment, in which the disparate images were presumably represented in opposite lobes of the brain. He accepts Charnwood's opinion that stereopsis under these circumstances occurs as a result of psychic appreciation of the motor fusional impulse elicited by peripheral retinal stimulation. (It seems that experiments like Morrison's do not deal at all with stereopsis in the purest and strictest sense of the word, since for this to be elicited images of small disparity must fall onto homologous halves of the two retinas—the temporal half of one retina and the nasal half of the other retina. This real stereopsis is, as has been well established, independent of exposure time, while in the experiments of Morrison exposure time was found to be a definite factor and as soon as greater exposure times were used all three subjects did equally well.)

Westheimer and Tanzman [142] made momentary (1/100 second) presentations of point targets seen in diplopia to several observers. Twenty different magnitudes of binocular disparity were used from 10 degrees "crossed" to 10 degrees "uncrossed," and 34 (68%) correct answers to 50 stimulus presentations were taken to constitute the 1% significance level beyond which guessing could be ruled out. Not all momentary presentations of diplopic images led to correct localization responses. The percentage of correct responses was 80% to 90% at 1 degree disparity, falling off to just a little better than guessing at about 7 degrees dis-

parity. Uncrossed disparity (to which the correct response was "behind the fixation target") was slightly more often correctly localized. The conflicting reports concerning the ability of an observer to localize diplopic images probably have their origin in individual differences of observers.

To measure the effect of viewing distance and target separation on binocular depth discrimination, Teichner, Kobrick, and Dusek [143] used two white 3 in. (7.5 cm.) square targets riding on hidden tracks. Observers had to set these targets at equidistance (into a subjective frontal plane) at different distances from themselves. The viewing distances varied from 10 to 100 ft. (3 to 30 m.), and the separation of the squares varied from ½ to 4 in. (1.25 to 10 cm.). The standard deviation of the settings increased (the accuracy decreased) with increasing viewing distance. On the other hand, the increasing separation of the targets affected the precision of settings only at extreme viewing distances and even then not in a consistent manner. The experiments confirm the well-known fact that depth discrimination decreases with viewing distance.

When fixation is transferred from one eye to the other in alternating squinters with harmonious anomalous correspondence after full correction of their deviation, either by prisms or with the amblyoscope or by surgery, a conjugated pendulum-like movement occurs, starting with a jerk in the direction of the eye which assumes fixation. According to Rotter,[144] this is the consequence of a discrepancy between the position of the eyes and egocentric localization. Both the surgical straightening of an esotropia and the correction of it by prisms or instrument produce a functional exotropia in the alternator, with only one of his eyes continuing to fixate at a time. The subjective straightforward direction remains anchored to an extrafocal area in the eye which does not fixate (even if in the new situation confronted with the fixation target). The change of fixation and of egocentric localization finds its expression in two opposing jerks before fixation is finally transferred.

TEPP (tetraethylpyrophosphate) is an insecticide used in dust form and distributed by aircraft. Pilots have long recognized the miosis which it causes. Some have also noted a decrease of light perception and, more rarely, an inability to judge distance. Experiments by Upholt, Quinby, Batchelor, and Thompson [145] show that it is unilateral contamination of an eye by spillage or other accidents which, by altering accommodation on one side, accounts for this occasional disability. Incoordination caused by faulty distance judgment might contribute a serious hazard.

Several authors have in the last few years studied the position in the space of the orbit of the vertical and horizontal ocular meridians during oblique oculorotations. Since these meridians supposedly carry the innate respective "local signs" of verticality and horizontality and must assume oblique positions in oblique oculorotations, it seemed to be a kind of mystery how vertical or horizontal contours could still appear horizontal or vertical when seen by an eye gazing in an oblique direction. The usual method of analysis availed itself of the afterimages of vertical and horizontal luminous contours produced in eyes in the primary position and "projected" with eyes turned into oblique directions. In latter years several authors have tried to solve the problem by a geometric analysis. Their work was recently reviewed by Miles.[145a] An exhibit by the late Dr. Joseph Pascal, at the 1955 meeting of the American Medical Association, dealt with the same subject, especially with the allegedly opposite torsion of the corneal and foveal meridians assumed by Márquez. The subject was once more reviewed by Linksz,[146] who comes to the conclusion that both retinal and corneal meridians always tilt in the same direction and in the sense of an extorsion whenever the gaze turns upward and outward or downward and inward, and in the sense of intorsion in the other positions.

Experiments carried out with perpendicular line elements under daylight conditions by Hillebrand in 1902, with very faint and

small lights in the darkroom by Blumenfeld in 1913, and, more recently, with so-called distorted rooms by Ames, have achieved quite unexpected significance through the work of the mathematician Luneburg, published in 1947-1950. Hillebrand found that the parallel appearing walls of an "alley," formed by two rows of vertical threads, are actually curved, and Blumenfeld found that the sides of a sagittally running "alley," formed by two subjectively parallel rows of small lights, not only are not actually parallel (in terms of physical measurements) but do not appear equidistant, i. e., the same distance apart at individual cross sections through the alley's full extent, when pairs of lights are scrutinized for separation in successive frontal planes. Upon these findings and some other peculiarities of binocular space perception, Luneburg founded a mathematical theory of binocular visual space which probably revolutionized thinking (and certainly caused the greatest possible amount of uneasiness in the minds of most of those working) in this particular domain of investigation. According to Luneburg's theory, the geometric characteristics of visual space are not Euclidian. (Whether this will prove to be correct or not, this very assertion made the seemingly faraway ideas of the mathematicians Lobachevski, Bólyay, and Riemann suddenly significant for all persons interested in space perception and fitted well with the fact that visual space—though boundless—is not infinite, as Euclidian space is supposed to be.) Even the mathematically most unsophisticated college graduate will by now have been at least exposed to some attempt at popularizing Einstein's theories and at least have heard about the curvature of space. He might have heard, furthermore, that this "curvature" may be "positive" (also called "Riemannian" or "elliptic") in a manner as lines on the two-dimensional "space" of a globe are curved or "negative" (also called "Lobachevskian" or "hyperbolic") in the manner of curved lines embedded into the two-dimensional surface of a hyperboloid or a saddle. And he also might have heard that, in fact, two great schools of cosmology are at grips at present to decide if the space of our Universe is of the one or the other type of curvature, having found for sure that it is not Euclidian. Now we have it on Luneburg's authority that visual space is also non-Euclidian.

In such spaces, of course, straight lines in the Euclidian sense are nonexisting. They are substituted for by so-called "geodesics," the shortest distance, between points in the particular space. It is by the characteristics of these "geodesics" that mathematicians decide whether a space is Euclidian or not and, if not, of what curvature. The nature of the curvature of such lines, of the "visual geodesics in binocular space" is the topic of a paper by Squires,[147] who repeated the just-described "alley" and "equidistance" experiments of Hillebrand and Blumenfeld under daylight conditions, arranging small squares of cardboard instead of threads or lights. For three of his four observers, Squires reports, parallel alleys were objectively farther separated than equidistance alleys. In other words, the individual pairs of small squares which formed an "alley" had to be brought closer to each other when separately scrutinized for equidistance, while Blumenfeld and other experimenters (Hardy and associates, Blank, Shipley) who repeated his experiments after Luneburg turned attention on them (to be sure, only under scotopic conditions, using small isolated spots of light) have generally found a reversed relationship. The implications of this controversy cannot easily be explained. Surely it is of significance for the problem brought to the fore by Luneburg's work. Squires' conclusions as to the nature of binocular visual space (that it has been proved to be "Riemannian" rather than "Lobachevskian") will not be easily accepted by those few conversant with these problems. It seems that some of his subjects gave different answers depending on attitude. It is furthermore certainly not easy to abstract from the experiential clues of ordinary vision in experiments under daylight conditions. On the other hand, most of our ex-

periences of spatial relationships obviously are given to us under daylight conditions and a generally acceptable geometry of visual space should not entirely depend on perception of relationships between just visible spots of light in otherwise complete darkness.

The fact, of course, that the geometry of visual spatial relationships is not the same geometry as that of objective space has long been known, and at this 100th anniversary of Helmholtz' "Handbuch" one does well to remember that ever since Helmholtz' studies it has been known that objectively straight frontoparallel point sequences do not appear straight subjectively.

Luneburg not only concluded from meager experimental material that visual space is "hyperbolic," its curvature being negative (the reader is once more reminded of the curvatures of a saddle), but also that there are two personal constants which characterize the subjective space of individual observers. One of them he called σ, and it supposedly is a numerical expression for the degree of depth perception a person might possess. The other, called K, is the numerical characteristic of the curvature of the observer's space. The experiments of Zajaczkowska [148] seem to add confidence to the reliability of the still much-too-theoretical magnitudes. She found that, in general, σ is greater in persons with good depth discrimination, while K indicates by what factor a person's visual space differs from Euclidian space.

Possibly the most important part of Luneburg's work is a method of transformation which is independent from the validity of his assumptions on the geometric nature of visual space and the just-mentioned subjective "constants." That objective and subjective space ("visible" and "visual" space, *Gesichtsraum* and *Schraum*) are not identical has long been known and generally accepted, but Luneburg showed an elegant and simple mathematical way by which certain magnitudes of one can be "transformed" into magnitudes of the other, especially how subjective spatial clues can be expressed or at least characterized numerically by magnitudes determined in objective space. (This of course is also not fully new since, e. g., the above-mentioned frontoparallel plane of subjective space has always been described in terms of objective space, although investigators realized that it does not "coincide" with the objective frontoparallel plane. The so-called Hering-Hillebrand deviation of the frontal plane horopter from the Vieth-Müller horopter circle is a magnitude expressed in terms of objective, or visible, space. Still, it characterizes the geometric loci of a visual "geodesic," a straight line in subjective space.) To mention only the most important elements of it, in Luneburg's system of spatial transformations, the physical y-axis (the line which connects the points of rotation of the two eyes) and the physical x-axis (the perpendicular at the just-mentioned line in the midpoint between the eyes) coincide with the axes η and ξ (the subjective frontal and the subjective straightforward directions) of visual space and the angle ϕ of physical space (the measure of the asymmetric convergence of the eyes when looking sideways at some object) is identical in magnitude with the angle ϕ (the angular inclination of the position of a visual object relative to the subjective straightforward direction) of visual space. Besides these coincidences and identities, the most important connecting links between visible and visual space are two values, γ and ρ, the first the angle of convergence between the eyes or, more accurately, between their principal lines of direction, the latter the subjective distance of the point of fixation viewed under the particular angle γ. (This rather dogmatic statement, while pivotal for Luneburg's theory, is certainly of at least doubtful validity, since the angle of convergence γ is generally accepted to be a rather poor clue of subjective, experienced, absolute distance. Certainly it is a clue only up to a very limited range and the mode of our determination of subjective absolute distance is still a mystery or, at least, a matter of controversy.)

In a set of experiments on the so-called frontal plane horopter, Zajaczkowska replaced the famous three bars of Helmholtz by three lights. Two of these lights were fixed at symmetrical angular distances $+\phi$ and $-\phi$ to the right and left of the Luneburgian x-axis, and a center light in this axis was moved until the three lights appeared in the same subjective frontal plane. The distances X_0 at which objective and subjective frontal planes coincided varied between 44 and 145 cm. for nine observers and showed good correlation with σ, meaning that in persons with good binocular vision the distance of X_0 was greater. At further distances than each individual's personal X_0 the center light had to pulled nearer than the lateral lights to appear in a plane with them; at shorter distances it had to be pushed farther away. (Of course, this is only added proof for the accuracy of Helmholtz' findings in his three-bar experiment, but it does not give any information about the "horopter," which the author asserted that he had studied. In Hering's frontal-plane horopter experiment the eyes are to be kept fixated at some point X in the x-axis and the lateral rods, or lights, are to be moved until they appear in the frontal plane through the subjective counterpart of X. Convergence and the position of the eyes are fixed and to be kept fixed in the true horopter experiment.) Zajaczkowska also repeated Blumenfeld's alley experiments, and her data agree with his, not Squires', results.

Another, simplified, alley experiment was carried out by ten Doesschate and Kylstra.[149] To produce a "parallel alley" these investigators used actual metal rails of 340 cm. length coated with a fluorescent paint and viewed in a dark room. The nearest point of these rails was at a distance of 150 cm. from the observer, 100 cm. below his eye level. Both were symmetrically located to the right and left of his sagittal plane. As expected according to the theory of central projection (and known to everyone who ever stood between the rails of a railroad looking at a distance), the rails did not give the subjective appearance of parallel lines but seemingly converged toward a vanishing point. The position of this point could be determined for each observer and was marked on a wall at 8 m. distance by a small "muscle" light. Another fluorescent rail, placed outside the two original ones and parallel to them, did not appear to converge toward the same vanishing point but toward a point more to the same side (which is against theory). A curvature in these objectively parallel rails was not noted (though expected in view of the above-mentioned results of Hillebrand and Blumenfeld and all the other investigators who since Luneburg have turned to the "alley" problem). Of course, ten Doesschate and Kylstra did not use disembodied lights under scotopic conditions but actual straight and parallel pipes, so that experience must have interfered. In order to evoke the impression of one common vanishing point, the third rail had to be displaced with its nearer end temporally. From the magnitude of this displacement one could calculate the distance of the vanishing point and this, according to the authors, determines the radius of the visual space of the individual observer. It varied between 9 and 28 m. Of the several explanations offered for this, one seems to be most plausible. Simple calculation will show that the change of convergence in looking from the far to the near end of the two objectively parallel rails is maximum in the case of their symmetrical placement on the right and left of the observer's Luneburgian x-axis, while in the case of two parallel rails on one side of him the change of convergence becomes less and less as the pair of rails is placed further from the midline. Should, as is thinkable, the sensation of parallelism of an alley depend on some associated magnitude of change of convergence from the alley's far end to its near end, then two parallel bars will have to be separated on the near end in order to appear parallel, if they are to the side of the observer. Much was, in these experiments, dependent on attitude. The rails could be perceived as parallel when they were really

parallel, but then they had no vanishing point. If all three rails were made to appear to vanish toward one point, the impression of parallelism was gone. Two experienced pilots appraised the situation best and needed least adjustment to achieve the impression of a common vanishing point. Their visual spaces had a radius of 52 and 105 m., respectively, much greater than those of all the other observers.

A short discussion of Luneburg's "brilliant hypothesis" is included in a paper by von Schelling on the "concept of distance," the mathematics of which, in general, is beyond the reach of an ophthalmologist. It deals with another fundamental concept of Luneburg's, the "invariance" of subjective space, its independence from eye and head movements. According to von Schelling's [150] analysis, the two eyes, the fixation point, and the fixed center of rotation of the head form a tetrahedron which is the subjectively fixed frame of binocular geometry. Since in "affine geometry" (the type of geometry in which the author has chosen to discuss phenomena of space perception—and even of color vision—and which is hard to define in this connection except by stating that it allows one to carry over defined magnitudes from one set of coordinates into another related, or affined, set) any tetrahedron can be changed "by affine transformation" to any other tetrahedron, binocular visual space should be "invariant to," and binocular vision independent of, head and eye movements. This, he thinks, it most likely is to a very great extent, but the author himself feels that "the interchangeableness of eye and head movements cannot be complete." The frontal plane (through the eyes) is to von Schelling the fundamental plane of binocular space. In it, "the type of the fundamental conic section" depends on the distance between observer and fixation point. Some change "from real to imaginary" occurs at about 5 ft. distance. (To me, not too conversant with advanced geometric vernacular, the latter two statements seem to allude to the change from concave to convex frontal plane horopters in Hillebrand's classic description.) Interestingly, to von Schelling the much-discussed alley experiments of Blumenfeld "prove next to nothing in connection with Luneburg's theory." Some of his concluding remarks are worth quoting, even if, out of context, they can only be partially understood: "For a given fixation point the metrics of the binocular visual space are non-Euclidian, at least in the neighborhood of the fixation point. Whether this is correct for the whole field of vision is not absolutely sure. . . . The particular metric depends on the momentary Euclidian distance between observer and fixation point. This . . . restricts seriously the applicability of the theory since normally the eyes roam continually from points farther away to points in the foreground. But it is at least probable that the momentary metrics of the binocular visual space are of the non-Euclidian type. . . . This sounds surprising. In the historical development as well as in our personal learning the Euclidian geometry comes first. But it should not be forgotten that the basic theorems [of Euclidian geometry] do not refer to vision but to touching. . . . The famous prisoners of Plato's Republic, their eyes fixed to the shadows on the opposite wall, might have developed a non-Euclidian geometry first. . . ."

The deviation between what is called the empirical horopter (the physical counterpart of the subjective frontoparallel plane) and the theoretical horopter, or Vieth-Müller circle, is, according to Halldén,[151] not necessarily the result of asymmetrical distribution of corresponding retinal points. It might be caused by dioptric asymmetries of the eyes. Halldén assumes that the optical axis of the eye (the line running through the second ocular nodal point and the fovea) does not coincide with the geometric axis of the retina (the line running from the second ocular nodal point through the center of curvature of the retina, the geometric center of the retinal sphere). Thus, even if Helmholtz' criterion is valid—in other words, even if points which are the same distance from the foveas (and in the same direction)

are pairs of corresponding points—the horopter will still deviate from the Vieth-Müller circle. The deviation will depend on the size of the angle δ between the just-defined two lines. Since Ogle's publication on this subject, one usually refers to a constant H as the characteristic of the so-called Hering-Hillebrand deviation from the Vieth-Müller circle. While Ogle expressed its magnitude as the relation of the differences of two anterior nodal point angles (the two angles subtended between the fixation point, the peripheral horopter point, and the respective anterior nodal points of the two eyes), Halldén expressed this same value H as a function of the just-described asymmetry, in other words of δ. In case the posterior nodal point distance to the retina is assumed to be 16.72 mm. and the radius of curvature of the retina is assumed to be 11.33 mm.,† then $H = 0.96 \sin \delta$. In case H is found to be 0.10, the value of δ would be about 6 degrees.

(Whatever the value is of such theoretical studies finally to solve the riddle of the horopter, one thing seems to be sure from the computations. One has so far always assumed certain inaccuracies to be negligible. In the work of the classic authors, the anterior and posterior ocular nodal points are usually assumed to coincide not only with each other but also with the center of curvature of the retina. They are even assumed to coincide with the center of revolution of the eye. Luneburg even went as far as to reduce the eyes to points L and R on the interocular axis, as far as all his calculations were concerned. This might be the source of some error, and more experiments might be necessary to solve the problem of the shape of the horopter. With modern instrumentation and modern calculating machines it should not be impossible once more to repeat the nonius horopter experiment—the only one having any justification to be called an experiment empirically to determine the horopter—and find its relation to retinal geometry. Of course, as long as experimenters continue to confuse the subjective frontoparallel plane, this intellectualized secondary structure of sensory space, with the horopter, no real progress can be expected in this field anyway.)

The relationship of physical and visual space, especially of the discrepancy between physical curvature and perceived curvature, is the subject of a paper by Fry.[152] It is almost impossible to review this paper without referring to formulas, since the argument is one of analytical geometry. (An abstract with comments has been prepared by me for *Survey of Ophthalmology*.) Assuming, as Luneburg did, the coincidence of the axes of physical and visual space, the equality of physical and visual distance (measured from the observer), and the equality of the physical and visual angles in which object points are, and are seen, to the right or left from the objective and the subjective straight-forward direction, respectively, Fry develops a number of interesting equations, relating to each other the horopter and its visual counterpart, the Vieth-Müller circle and its visual counterpart, the frontoparallel plane and its visual counterpart, and, finally, the curvature of the latter and its perceived distance. (Unfortunately, the horopter, especially its form, is nowhere defined. All we learn is that it is the locus of points in physical space which form images on corresponding parts of two retinas. For all this the horopter could very well coincide with the Vieth-Müller circle, but, without knowing why, we are just led to assume that it is not.)

Fry's conclusions are, no doubt, strange to those trained in biology rather than mathematics, psychology, and optometry, and, in the great controversy over "innate" and "experiential" which has been going on since the times of Johannes Müller and Helmholtz, Fry is certainly on the side of an experientialism to which the three papers [128-130] reported in this section certainly give no succor. For Fry, spatial relationships are learned. He believes that "a person learns to perceive differences in distance

† These are the values given by Lo Casa in 1923.

by using his hands to hold one object at the point of fixation and a second object at some other place and by noting the relationship between the disparity of the retinal images perceived through the eyes and the displacement of the object perceived through the hands which makes perceived distances actually equal to physical distances." After a person has used his hands to learn the relation between retinal disparity and the displacement of points in the sagittal axis in front or in back of the point of symmetrical bifixation, Fry believes "he can use this learned relationship to evaluate the displacement" of any other point in the fixation plane in front of or behind a point on the horopter having the same lateral declension, using for this as a clue the disparity of the retinal images of that point. If he can evaluate the distance of the point seen in symmetrical bifixation (the Heringian *Kernpunkt*) on any bases whatever, he can use this information about the disparity of the retinal images of points in front or behind. "Essentially the job which the brain must perform is to associate with each value [of the perceived distance of the point of bifixation in symmetric convergence] a surface of a certain curvature as representing the counterpart of the horopter in visual space and then objects in front or behind the horopter are perceived in relation to the counterpart of the horopter in visual space."

"The counterpart [of the objective frontoparallel plane] in visual space is convex to the observer. The amount of convexity will depend upon its perceived distance . . . and since the eyes must learn to associate certain curvatures with certain distances perceived curvature and perceived distances become interchangeable quantities."

While Fry's analysis of visual space remains within the confines of Euclidian geometry (as a matter of fact, in a previous paper he came out straight for the Euclidian nature of visual space), he comes to the same result as Luneburg, at least in one significant point. He concludes, on the basis of some brilliantly developed equations, that points on the Vieth-Müller circle appear equidistant to an observer, while objectively they are obviously not. This, as Fry emphasizes, means that the distance of peripheral objects in the plane of regard is overestimated with respect to objects in the center of the field. "This overestimation of distance is essential in helping peripheral objects appear to maintain a constant fore and aft dimension as they move in fore and aft direction." In a second paper on the same subject, Fry [153] tries to prove that the same overestimation occurs in the median plane as well and that this permits spherical or plane surfaces which are normal to the sagittal axis to appear to have constant curvature in the horizontal as well as in the vertical direction.

The significance of a long paper by Gillott [154] rests not in any new information it would give to those familiar with the subject of aniseikonia but in the well-rounded picture it offers of many of its aspects. Since it appeared in a British magazine, it is hoped that from now on information about measuring aniseikonia will become more easily available to non-American readers. What, however, makes this author's work remarkable is a technical contribution. Not having any of the American instruments at his disposal, Gillott built not only his own direct-comparison eikonometer (at least a simplified haploscopic model of it) but also a complete and seemingly excellent space eikonometer, including measuring head, geared size lenses (to determine the declination error), and variable magnifying units. He not only describes the pertinent optical principles on which these devices rest but also gives sufficient manufacturing detail so that anyone who cannot afford to buy the commercially available, expensive, instruments is, with some mechanical talent, able to duplicate the author's work. The main obstacle so far for a more general use of eikonometry outside the U. S. has been the inability of physicians in foreign countries to avail themselves of the instruments offered. This obstacle is now removed. Having made the variable magnification units for his instrument, Gillott,

furthermore, devised simple methods to test the accuracy of these units and to calibrate them. This also can be easily duplicated. Basing his description especially on Ogle's classic work and his many technical contributions, Gillott gives an easily understandable description of how the information supplied by the space eikonometer (vertical and horizontal size difference and declination error) can be translated into terms of a correcting size lens. His excellent and short introductory historical note deserves especial mention.

Technical information for those who dare to tackle the problem of computing and ordering (or grinding) their own correcting size lenses is now also available in an unpublished laboratory manual by Bechtold. This is certainly not easy reading. We of this Western hemisphere who are fortunate enough to have the know-how of the manufacturer at our disposal will hardly need to plow through its pages. Again, it is mostly our European friends and the European optical industry who might receive some new incentive from this work to do something about an important but neglected problem (So far, it seems that only the late Lord Charnwood dared to compute and grind his own corrective size lenses. However, he restricted himself to calculating only individual lenses.) In Bechtold's manual appropriate tables are found with the help of which everyone interested can, after some study, both compute the "spurious" magnification inherent in the individual's refractive correction and determine such curvatures and thicknesses of dispensed lenses as will correct at least the simpler types of the aniseikonia found in the eikonometer. After these computations every well-equipped prescription laboratory should be able to grind these lenses. Of course, for very complex lenses (bitorics, laminated lenses) one would still have to turn to the computing and grinding facilities of the manufacturers.

The only other paper of some interest relating to the subject of aniseikonia is a clinical communication by Schapero [155] on a case of recurrent corneal dendritic ulcer of one eye which changed the astigmatism of this eye from −0.75 D. to −3.75 D. and the axis from 15 to 60 degrees. The patient was acutely aware of the distortion of the retinal image by this rather sudden change of refraction. He turned out to be an excellent subject for testing in the space eikonometer and experienced great relief from appropriate correction.

VII. Oculorotations, Convergence, Accommodation

After careful experiments, Tani, Ogle, Weaver, and Martens [156] finally concluded that a "precise objective determination of eye movements by photographic and telescopic observation of details on the eyes themselves or of images from light reflected from the corneas is not possible." For the same reason, they also found it impossible precisely to measure the extent of the perimacular fusional areas. Precision of measurements was, in their experiments, made impossible by a displacement of the corneal reflex images—the very clues which in their experimental set-up were supposed to give objective data on ocular movements. The discrepancy must have been caused, the authors think, by the failure of the eyes to turn around fixed axes. It seemed likely, from their analysis, that during convergence the eyes were displaced nasally and forward and that in the production of this displacement the synergistic action of the oblique muscles might have played some part. The tonic state of the muscles as modified by forced convergence or divergence and by accommodative reflexes introduced a variability in the translatory displacements which prevented the determination of any lawful behavior of the eyes under conditions of stress.

Looking for the stimuli which cause involuntary drifts and saccadic eye movements, Cornsweet [157] found that during normal fixation it is the instability of the oculomotor system which permits the eyes to drift. As the retinal image drifts away from some particular part of the retina, it becomes more and more probable for a saccadic mo-

tion to appear, the effect of which is to return the retinal image to this particular point. The frequency of drifts is not changed by the absence of a fixation point. However, when there is no fixation point the eyes are turned farther and farther from their mean position by random drifts. This circumstance proves, according to the author, that saccadic movements are under visual and not proprioceptive control and that they and not the drifts hold the eyes on their target. No visually controlled smooth movements occur during monocular fixation. Pursuit movements were first believed by the author to be possibly composed of saccadic movements. Further experiments showed, however, that under conditions set up for pursuit movements smooth tracings do occur. This proves, according to the author, that pursuit movements are not a succession of saccadic movements.

Experiments by Westheimer and Mitchell [158] with artificially produced crossed and uncrossed disparities of variable magnitude convinced the authors that convergence movements follow immediately as soon as required by the production of appropriate horizontal disparities. The reaction time was found to be 0.15 to 0.20 seconds. "Convergence relaxation" (divergence) responses are, on the other hand, much slower. Sometimes no response takes place, and occasionally a tentative response is made in the opposite direction after a long reaction time. A 1.5 degree convergence takes 0.4 seconds to be completed. Higher degrees take longer, and the final limit of convergence is usually a degree or so less than required by the stimulus. These higher degrees of convergence stimuli are answered by a biphasic response as if a first burst of convergence (the degree of which is not related to the degree of disparity) were followed by a second burst in order to undo the still remaining disparity. However, there is also a possibility that the diphasic character of the reaction shows that accommodative convergence superimposes itself upon the fusional convergence elicited by the disparity and that the two forms of convergence have different time characteristics. The differential behavior in regard to the requirements of convergence and convergence relaxation once more convinces the authors that one has "the ability to distinguish crossed from uncrossed diplopia." They conclude that "the differences in responses seem to be due to a genuine difference between the mechanism of convergence and that of convergence relaxation."

The authors extended their study upon stimuli requiring asymmetric convergence. Responses to these they found to consist of two parts—a conjugate saccadic movement and a convergence factor. They assume that the eyes first make a saccadic movement without change of convergence until the bisector of the angle of convergence passes through the new fixation point and that upon this saccadic movement there is superimposed a convergence movement of different time characteristics.

It seems that the fundamental electromyocrographic studies of Breinin on the extraocular muscles have again drawn attention to the behavior of the eyes during asymmetric convergence and the applicability to this movement of Hering's law of equal innervation, as two other extremely interesting and well-presented papers by Alpern and Ellen [159,160] also deal with this problem. These authors, with modern equipment, repeated (and, of course, found confirmation of) one of the earliest psychophysiologic experiments first executed by the great Johannes Müller. They found, in other words, that if one eye is made to accommodate from a far to a near target (both along the same line of direction) while at the same time the other eye is occluded, the covered eye makes a nasal (convergence) movement. The tracings of the movement of the covered eye indicated smooth continuous rotation. There was no trace in the graphs of a separate accommodative-convergent and proximal-convergent impulse. The tracings showed, furthermore, that the fixating eye, to which the accommodative stimulus was presented, did not move at all. At least

it did not move as long as the other eye was occluded.

Different results were obtained by another type of experiment, in which fixation was binocular, although the near and far targets for the stimulation of accommodation remained aligned with one of the two eyes. In this case it seemed that Hering's and Bielschowsky's interpretations were valid and that the eye aligned with the far and the near target would partake in both the vergence and the version necessary for the change of fixation. These movements added up to zero displacement, but the eye was not motionless.

The authors offer an interesting hypothesis to explain the difference found under the two sets of conditions. They believe it possible that in the original Müller experiment (that is, under the conditions of monocular fixation) there is only a change of accommodative signal. In this case, somatic muscular innervation prevails over autonomous innervation and thus the fixating eye remains motionless, while the occluded eye turns. Under the conditions of the second experiment there occurs a displacement of the fixation signal in the nonaligned eye as well as a change in accommodative signal, and thus both somatic and autonomous impulses reach both eyes, the aligned eye as well as the not-aligned eye, causing irrelevant movements of the former with the zero end-result.

The tracings of the movements of the occluded eye were finally submitted to a thorough analysis. The authors determined the latency period, duration, amplitude, velocity, and acceleration of these rotations under conditions of varying accommodative demand. The amplitude of the rotations increased first with increasing separation of targets, but there seemed to be a limit to this amplitude—the convergence lagging behind requirement when the latter became too great. Both the average velocity and the average acceleration increased with increasing demand, so that the total duration of the individual rotations increased only a little. In fact, the duration of the individual oculorotations turned out to be fairly independent of the required amplitude.

Using the technique described by Marg, it was found by Alpern and Wolter [161] that during so-called saccadic movements (the quick movements by which the gaze is transferred from one fixation point to another) the velocity of rotation of the eyes is higher than 400 degrees per second, while the average velocity of vergence movements is approximately 8 degrees per second. Dodge, in his classic description of the types of ocular rotations, had noted already that eyes are able to carry out saccadic movements and vergence at the same time, in case the change of fixation requires both. Breinin's electromyographic studies suggested that when they are of opposite direction these movements cancel each other out, while the experiments of Alpern and Wolter indicate that, in an abortive manner, both are present. For the explanation of the fact that under a single change in fixation both saccadic and vergence movements can occur, the authors refer to some recent histologic studies of Wolter on the innervation of the eye muscles by two (as a matter of fact, three) different types of nerve fibers, viz., myelinated nerve fibers with motor end-plates and more delicate nerve fibers ending with loops or a terminal network—the first being somatic, the latter two autonomous in character. The authors suggest that the fast saccadic component might be initiated through the somatic fibers, the slower vergence component through the autonomous nerve endings. This attractive hypothesis would certainly explain the very close similarity of the time characteristics of the vergence movements (convergence) and the contractions of the intraocular muscles (accommodation), which are involved in the near reaction. It also would make it understandable how an eye muscle could carry out one yoked movement together with a muscle of the other eye and at the same time partake in another movement synchronized with the antagonist to this latter muscle—both during the same change of fixation.

A delightful experiment on the effect of alcohol upon fusion reserves and stereopsis was carried out by Seedorff.[162] "The seven subjects met at 7:00 p.m. and cocktails were served at once. Then they had Danish sandwiches, beer and schnaps, followed by coffee and brandy. Later on they continued with whiskey. The party took place in a private house and went on until 2:00 a.m. The ocular observations were performed prior to and at suitable intervals during the experiments." The subjects were also tested at 9:00 a.m., 3:00 p.m. "to record the effect of a possible hangover," and again 24 hours later. In association with the ocular tests, suitable blood samples were obtained. The author confirmed that inebriation gives rise to esophoria and found that motor fusion reserve deteriorates. It also seemed that stereopsis became poorer. However, the experimental set-up was too primitive to allow any accurate measurements of quantitative changes. The author also confirmed the important findings of Bárány and Halldén that normal retinal rivalry suffers in alcoholic intoxication. The presence of nystagmus in the experimental subjects is explained "as a result of action of alcohol upon the vestibular organ and the cerebellum with secondary involvement of visual integration." The well-known dizziness and diplopia of intoxicated persons is easily explained on the basis of these findings. All these effects lasted for several hours after the alcohol intake.

That nystagmus occurs after the intake of alcohol, that in fact it seems to be the first sign produced by it, was also found by Howells.[162]

To measure the near-point of accommodation even when visual acuity is markedly reduced, Sloan and Habel [96] devised a simple instrument based on the principle of the Badal optometer. Their instrument provides for any desired change in the apparent distance of the test object without associated change in the size of the retinal image. It consists of a +16.00 D. lens located at a distance so chosen that its posterior focal plane coincides approximately with the anterior focal plane of the eye. A test target can be moved in front of the lens, and its approach in calculated steps calls for ocular accommodation of known amounts.

Possibly the most important additions to our knowledge of accommodation since the publication of the fundamental work of Fincham are the several studies by Heath [164] on this complex subject. Starting his discussion with Maddox' classic subdivision of convergence, Heath emphasizes that this classification is purely operational. Maddox' different types of convergence (tonic, accommodative, proximal, and reflex) are, according to Heath, "simply quantitative variations in the response to qualitatively different stimuli rather than qualitative differences." Thus, his analysis "avoids the need for hypothetical 'centers' or 'preemptive' pathways for each of several slightly different 'functions'." This wholesome way of avoiding the hypothetical "centers" and "pathways" leads toward an analysis of the accommodation function of exemplary intelligence and the resolution of such seeming contradictory experimental evidence as that offered by Marg (who believed accommodation to be a primarily voluntary act) and by Fincham (who found it almost wholly reflex, consisting of an associated reflex to convergence and a direct response to the vergence of light). Making an operational analysis of accommodation, Heath finds much evidence against Fincham's theory. Using blurred targets, he found that with increasing blurriness of contours normal observers became more and more incapable of responding to changes of vergence of rays, and he thinks that reflex accommodation is a response to contrast gradients. He finds that this reflex component of accommodation is of such importance as to prevent, in the presence of fine and sharp detail, other stimulus forms from becoming effective. It makes it, e. g., extremely difficult to measure convergence accommodation, the presence of which is generally taken for granted. Heath finds convergence accommodation to be of little significance and easily forestalled by reflex accommodation, while Fincham be-

lieved the amount of convergence to be the main or "coarse" determinant of accommodation, at least in binocular vision. As to proximal accommodation, Heath suggests its identity with voluntary accommodation. The observer "thinking of near" elicits sometimes large accommodation changes. But only the thinking is voluntary; the accommodative change is automatic. The last factor, the tonic accommodation of the "relaxed" eye, is given by the difference of accommodation from zero which is found whenever the eye receives no specific stimulation to cause it to focus upon an object. This tonic accommodation is, according to the author, the cause of so-called night myopia, of the myopia of the totally color blind, the increased refraction of the eye when confronted with a blurred target, and the space myopia of flyers and aircraft spotters. It is being inhibited whenever there are sharp contours to focus upon.

A well-presented study by Heath [165] deals with the accommodation responses of the totally color-blind. Three patients were examined. They were suffering from what is called typical total color blindness and had a visual acuity of 20/200. Accommodative stimuli were produced with the Badal optometer (a classic French device which allows for continuous alteration of apparent distance), with a Snellen chart placed at various distances, and by placing concave lenses in front of the observer's eye. The accommodative response was objectively determined with a coincidence optometer. All three subjects were quite unresponsive to changes of stimulus, behaving like presbyopes. More surprising than the lack of accommodation was the apparent myopia of all of them. A similar type of "false" myopia was found by Heath in normal subjects to whom extremely blurred targets were presented and earlier by Whiteside, whose subjects viewed a bright and empty visual field. Both the near absence of reflex accommodation and the increased refraction found in these totally blind subjects are, according to Heath, the consequence of their low visual acuity and are unrelated to the possible absence of foveal or retinal cones, generally assumed to be the cause of typical total color blindness.

Accommodation and ocular tension are continuously regulated, according to van Lint and Alaerts,[166] by ocular cybernetics. The need for visual clarity stimulates the ciliary muscles, and the clarity of vision informs the muscles about the degree of exactitude of the accomplished act; they correct it, in case of need, in the measure of their possibilities. The "antagonistic automatism" of the Müller and Bruecke muscles assures, under normal conditions, the perfect functioning of the mechanism of accommodation and of the maintenance of ocular tension.

(It is interesting to see the new American term "cybernetics" appear in the French vernacular. Still, the mood of the paper is that of a dated biologic romanticism. With Fincham, Fry, Heath, and many others trying to find out what the stimulus of accommodation actually is, this paper on ocular cybernetics claims that it is the "clarity of vision" which "informs" the ocular muscles and the "need for visual clarity" which "stimulates" them.)

Hamasaki, Ong, and Marg [167] measured accommodation in 106 subjects between the ages of 42 and 60 years, by both the Donders-Duane ("push-up") method and by stigmatoscopy. The mean amplitude of accommodation measured by the first method was found to decrease rapidly up to the age of 50 or 52 years and then remained essentially the same up to the age of 60. The stigmatoscopic amplitudes were found to be significantly lower. The difference between the two findings is due to the depth of focus of the eye. The effect of this is an apparent addition to the amplitude of accommodation. In the stigmatoscopy method this factor is eliminated, and after the age of 52 accommodation turns out to be essentially zero. Increases of reading addition after this age seem to be beneficial only because of the added magnification factor. They do not make up for any further loss of accommodation.

Christofferson and Ogle [168] found that the ratio of accommodative convergence to change of accommodative stimulus (called the AC/A ratio) increases markedly in cycloplegia caused by homatropine. As the cycloplegia gains in effect, the ratio becomes increasingly larger. At the same time, at any given state of cycloplegia, it varies linearily with the change of stimulus. The ratio remains normal in presbyopia. Thus the cycloplegia of homatropine must be caused by a mechanism quite different from the mechanism of presbyopia. The accommodation-convergence association results from an unconditioned reflex ("a unit change in the stimulus to accommodation results in a unit change in the innervation to the convergence-divergence process"), and the synkinesis must result from an innervation which is directly proportional to the stimulus to accommodation. "It is the stimulus to accommodation which gives rise to the accommodative convergence," the authors conclude. It occurs whether the eye has actually accommodated or not.

VIII. Miscellaneous Topics

Leibowitz, Chinetti, and Sidowski [169] found that the constancy of form breaks down at short time exposures. An obliquely viewed circle appears to be a circle, although its retinal image has the form of an ellipse when the exposure time is long enough, e. g., one second. If this is cut down to 0.01 second, one sees an ellipse more in accordance with the physical image on the retina. Constancy of brightness is also affected, and in a similar manner. It, too, is more in accordance with the physical characteristics of the stimulus presented in very brief flashes. Perception of size seems not to be affected in the same way, as the authors found that about the same judgements of size are made over a range of 12 to 192 ft. (3.6 to 57.6 m.) both in continuous illumination and with light flashes of only 0.0005 second duration.

The purpose of a study of reading efficiency of school children by Shepherd [170] was to show that reversing of the order of letters is a widely manifest psychologic fault of young readers and not, as some investigators think, an expression of an anxiety situation or of "infantile reversion" (whatever this means). He found that the greater the tendency to reverse the order of letters the slower the reading speed, but he found no definite correlation between reading speed and eye dominance as such, though those of left eye dominance showed a discernible tendency to prolong a reversal pattern. His attack on the problem was formidable. Tests were made, in 809 school children, of the hearing by audiogram, the Snellen visual acuity at 20 ft. (6 m.), the near point of convergence, the span of recognition of letters and numbers at 1/1000 second exposure, the dominance of eyes (this was checked by five different methods), the hand dominance (tested by five methods), and the foot dominance (tested by four methods). Besides, 10 figures were given to them to draw and 10 symmetric patterns to copy. Mental acuity was obtained from school records and checked by the Kent Emergency Scale. Reading ability was tested by the Gray oral method and by the Sangren-Woody test. An interview was arranged for each child, and Dr. Moodie's check test was used as a guide for behavior.

All these children were tested in Kanawka County, in West Virginia. To minimize the effect of poor home conditions and low nutrition, the children chosen for this study came from neighborhoods of better economic status. Out of this group 313 were found to be well adjusted and from good homes. Their sight, hearing, and general physical condition were all good. They were all definitely superior in intelligence. Still, when tested for their reading ability (by the Gray oral test method) 113 (or more than 30%) were below the expected grade level. The only thing to which the author could correlate this reading difficulty was the approach of the children to free-hand drawing. Those of the children who did their outlines from right to left in more

than half of the objects drawn showed a greater number of poor grades and slower speed of reading.

The favorite assertion of psychologists that home difficulties and behavior problems are a major source of reading deficiencies certainly finds no corroboration in this study. Neither could it be shown that right or left eye dominance plays any guiding role in reversals. The efforts to change dominance by patching techniques or the so-called "Correct-Eye-Scope" are thus useless, and findings like those of Berner and Berner could not be confirmed. Significantly, the author feels that the whole method of intelligence testing in schools is put into a questionable place when it is found that 80 out of 809 children (almost 10%) are stigmatized by such testing as being of low intelligence, when by oral test methods they are found as being of actually superior intelligence. Such children simply are poor readers and then score poorly on the standard school tests because of this. He also makes some comments which in this time of the general upset about "Why Johnny Can't Read" certainly deserve to be well noted by ophthalmologists. "There is," as he writes, "a distinct possibility that the teaching of phonics might clear up a high percentage of both problems." "Present day teachers are inching back to phonics," at least "using the best of both phonic and word-as-a-whole method." "We ophthalmologists can and should take a hand in urging our school systems to take a positive stand on this matter, setting up a sensible plan of attack . . . and should look appraisingly into the school performance of the children we examine."

With illumination constant at 25 ft-c. and with 10- and 8-point reading type, measurements of reading speed were made by Tinker,[171] with the text held perpendicular to the line of sight, flat on the table, and 10 and 30 degrees, respectively, below horizontal, at the far end. In comparison with the perpendicular position, both types were read significantly slower at all other slopes. The retarding effect increased with the degree of the downward slope. The visibility of the type declined in similar manner. This research might have important implications for schools, libraries, and other institutions where reading is an essential part of activities.

There has always been some difficulty with the practical applicability of the much-cited classic results of Blackwell (1946) on contrast thresholds—a problem of great significance in human engineering—since only the mean curve of these thresholds was published and not the spread of values. The most important question, however, in many fields of practical application is not the mean value of the contrast threshold. Sometimes one has to know what contrast to apply so that practically everyone can see a stimulus detail. At other times one wishes to know what the requirements are so that a particular detail will be invisible to practically everyone. Fittingly, Vos, Lazet, and Bouman,[173] of the Netherlands Defense Research Council, found it important to reexamine visual contrast thresholds from this angle, using both black dots and Landolt rings on backgrounds of variable contrast. It turned out that training had practically no influence on the measured faculty.

Another factor of interest in human engineering but also in the daily practice of the perimetrist has been experimentally approached by Mertens.[174] When the probability of observation of a peripherally observable test flash is to be measured, one can either have special attention for the direction in which the flash is expected or have a general attitude of attention toward the whole visual field. The almost unexpected result of Mertens' observation is that when the gaze is fixed (as in perimetry) the probability of observation is practically independent of attention and that special attention in some expected direction is more fatiguing than just general attention.

Lowery's [175] paper deals with a problem of special interest only to the educational or industrial psychologist—the problem of the possible transference of one learned way of acting or skill onto some other field.

Still, some of the results may be worthy of a short note, since they reflect upon the role of vision in this process. In one set of experiments, subjects were instructed to make 100 taps at equal time intervals. This test was first made blindfolded and then under free visual observation. There was no significant difference in performance. Obviously, there existed little coordination between the "time sense" and vision. However, when a clicking device was attached to the key so that a sound was produced each time the registering key was depressed, spacing improved noticeably, indicating a correlation of significance between hearing and the "time sense." (By the way, the ability to time properly was greatly enhanced when the tapping was not uniform but followed some rhythmic pattern.) The role of visual control was much greater when the tapping experiments involved judgments of intensity rather than timing. The pen marks produced by tapping were much more uniform under visual observation than in the control experiments in which the subject was blindfolded but instructed to exert uniform pressure. After having been trained to exert uniform pressure in tapping under visual control, the acquired skill could readily be transferred to other tasks (e. g., the releasing of keys which required a certain amount of pressure to become effective, etc.). Still, the experiments prove that "vision is not in that exclusive sense involved in acquiring skills as was previously supposed."

In experiments by Kephart and Chandler,[176] subjects were required to control a movable pointer by means of an automobile steering wheel. The pointer had to be kept on the center of a moving road pattern. (Similar road patterns are to be found on the well-known devices of amusement parks.) While the subject tried to keep the pointer on the moving stripe, he was repeatedly shown a small white button on a perimeter-like device. The driving performance lasted 30 minutes; the visual span was tested at 12 equally spaced intervals during this time. The data were treated statistically. It turned out that there was a decrement of visual span of 60 to 20 degrees in the first two or three tests. After this the decrement levelled off to about 10 degrees and was actually increased by the interjection of a two-minute rest period. The data indicate that concentration of attention to a far point tracking task with consequent stress results in significant reduction of visual span.

The transmission of light through the ocular media of the rabbit eye was measured on freshly enucleated eyes by Wiesinger and associates,[177] using a Beckman spectrophotometer as light source and a Kodak Ectron cell as detector. The measurements extended from 390 to 1350 mμ, and the results showed that the transmission of the ocular media was practically the same as that of water or saline, except for the range below 490 mμ, where the transmission of the ocular media becomes considerable smaller. It is near 90% up to 920 mμ, shows a new peak (near 80% transmission) at 1080 mμ, and becomes practically zero near 1350 mμ. (Short infrared rays certainly reach the retina in sufficient quantities.)

Farrell's[178] book, "The Story of Blindness," is an enlarged edition of his Lowell Lectures, delivered at Boston University in 1953. The material of eight lectures of 50 minutes each has been expanded into a book of eighteen lectures, with an excellent index and many references. Farrell had at his disposal the facilities of the greatest collection of material on the blind, the library of Perkins Institution; the Massachusetts Eye and Ear Infirmary and the National Society for the Prevention of Blindness were helpful in preparing the medical side of presentation (and his story of retrolental fibroplasia is indeed most interesting), and the American Foundation for the Blind and the Massachusetts Institute of Technology gave him valuable information on all kinds of devices to aid the blind. Farrell's chapter on causes and cure of blindness will be of interest even to ophthalmologists and, besides, the book is crammed with interesting historical detail. We learn, for example, that it is exactly 100 years since Karl Siegmund

Franz Credé, the originator of preventive treatment of the ophthalmia of the newly born, became professor of obstetrics in Leipzig and how Dr. Hasket Derby, "fresh from von Graefe, Arlt, and Donders, felt that he represented the rising sun of science" and rebuked the professor of ophthalmology at Harvard, Dr. Henry W. Williams, for his admonition to physicians not to use silver nitrate. We also learn how, again, just 100 years ago, Albert Ely Beach, the editor of *Scientific American*, patented a process of imprinting embossed letters for the blind. The book is certainly well worth reading.

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Correction

In the article, "Electromyography—A Tool in Ocular and Neurologic Diagnosis: II. Muscle Palsies," by Dr. Goodwin M. Breinin, in the February issue (pp. 165-175), the legends for figures 12 and 14 were reversed.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON OPHTHALMOLOGY

Isadore Givner, M.D., President
Byron Smith, M.D., Secretary
Nov. 19, 1956

Induced Ocular Hypotony in Intraocular Surgery. NORMAN S. JAFFE, M. D., and DAVID S. LIGHT, M. D., Miami, Fla.

The use of digital pressure on the globe is not new. It has been used to promote a greater diffusion of anesthetic agents, to offset the effects of bleeding created by the retrobulbar needle, and now to lessen the incidence of vitreous loss by inducing a marked ocular hypotony. Dr. Paul Chandler is responsible for the latter observation and technique.

Following a retrobulbar injection of a lidocaine (Xylocaine), hyaluronidase (Alidase), and epinephrine mixture, pressure is exerted over the closed lids for three minutes. The pressure is relaxed every 30 seconds for 2 to 3 seconds. There is a precipitous fall in intraocular tension, usually to 0 mm.

The following observations are made during surgery: 1. The corneal incision is never followed by a gaping wound; in fact, the cornia collapses. 2. There is no sudden reduction of intraocular tension. 3. The iris assumes a more posterior position. 4. More hook pressure externally is required during the extraction. 5. The face of the hyaloid is concave; it does not rush forward. 6. The globe is often collapsed after surgery; the sclera may be indented. 7. The chamber forms more readily. 8. There is never a gaping wound after the delivery of the lens. 9. All maneuvers are made with far greater safety (such as removal of retained capsule fragments and postdelivery suturing).

An experimental lens extraction on a patient with two blind eyes was performed with use of this technique. A Graefe knife was thrust into the vitreous. There was no gushing forward of vitreous. The hyaloid was concave and posterior.

A case of marked adherence of the hyaloid to the lens was encountered. The lens forceps was removed, and an erisophake was substituted. The lens was lifted and the hyaloid was peeled from the lens without loss of vitreous.

Nine consecutive intracapsular cataract extractions were performed on patients between the ages of 25 and 35 years, not remarkable, but worthy of note.

Ten penetrating keratoplastics have been performed with use of digital pressure. The hypotony facilitates direct suturing but makes the trephine section slightly more difficult.

There was only one instance of vitreous loss in 125 cataract extractions, and this occurred in a high myope.

The possibility of expulsive hemorrhage is probably much lessened, owing to the initial lowering of ocular tension.

This technique has no effect in lowering the tension in acute narrow angle glaucoma in the uncompensated phase. After the tension is controlled medically it can be further reduced by use of a retrobulbar injection and digital pressure.

An important bit of evidence is as follows: If the wound gapes after a corneal section (when this technique is not being used), a broad spatula placed on the cornea will press the lens against the hyaloid. After three minutes of pressure the wound will no longer gape (Vail). This must be due to decreased intravitreal pressure, since there is no aqueous after the section.

The mechanism of hypotony may be summarized as follows: The retrobulbar injection results in a lessened inflow due to parasympathetic block, and the digital pressure "milks" out the excess intraocular fluid.

Symposium on Prevention of Complications in Ocular Surgery

Corneal Surgery. RAMON CASTROVIEJO, M. D.

Corneal surgery, including the several types of keratectomies with or without plastic repair of the conjunctiva, with or without buccal mucous membrane graft, and the different types of lamellar and penetrating keratoplasties, has become a highly specialized field of ophthalmic surgery, requiring training under expert guidance in order to master it. Improvization on the part of the surgeon without adequate training and the use of inadequate instruments will result in complications at the time of the operation or during the postoperative recovery.

It is therefore essential, in order to prevent complications, that the surgeon be acquainted with the indications for the different types of corneal surgical procedures, to have developed the ability to perform the different techniques in animals before undertaking the performance of the same operations on human beings, and to use first-choice instruments in as perfect condition as possible.

In the present state of corneal surgery, in operations upon favorable eyes, the number of complications should be few and infrequent during either the operation or the postoperative recovery. There are, however, very unfavorable cases in which complications are unavoidable and yet the operation is justified so long as it will offer the patient with very precarious vision even a remote possibility of improvement.

The surgeon with good clinical and surgical judgment should be able to predict when complications are likely to occur and take the steps necessary to prevent them or, if they are unavoidable, to minimize their seriousness.

Corneal surgery requires the accurate measurements in tenths of a millimeter in depth or in width, and it is of extreme importance to have the operating field well illuminated as well as to use magnifying spectacles in an effort to improve operative accuracy.

Preoperative Measures.—To prevent the possibility of systemic complications or pathology affecting the postoperative recovery of the eye, the general condition of the patient must be improved as much as possible before ocular surgery is carried out.

If the area surrounding the patient's eye has some skin infection or irritation, it should be cleared before operating upon the cornea. Pathology of the eye other than that affecting the cornea, such as blepharitis, trichiasis, entropion, ectropion, conjunctivitis, iritis, and iridocyclitis, should also be adequately treated before the cornea is operated upon. Glaucoma, particularly, contraindicates corneal surgery. Therefore, it is essential to normalize the tension of the eye by medical or surgical methods before any surgical procedure is carried out on the cornea. If the cornea itself is inflamed, surgery is contraindicated unless the operation is performed for therapeutic purposes, such as in an eye with a corneal perforation or a chronic ulcer which fails to cicatrize by nonsurgical treatment.

Anesthesia.—General anesthesia should be employed in highly nervous patients, in children, and in long procedures such as keratectomies with conjunctival plastic repair, where usually densely vascularized cornea and conjunctiva is accompanied by irritable eyes and pronounced photophobia, in order to prevent the complications which may arise from a very uncooperative patient. The use of direct suturing of the borders of the graft to the cornea of the host in keratoplasty has greatly minimized the danger of complications which were formerly observed when patients developed postoperative coughing under general anesthesia. The direct suturing of the graft to the cornea of the host has permitted, particularly in children, the performance of keratoplasties without limitation as to age and with no greater number of complications than those observed in adults operated on with use of local anesthesia.

Adequate sedation before the operation should result in a high number of quiet, cooperative patients who can be operated on under local anesthesia. For local anesthesia in corneal procedures it is advisable to use anesthetics that will not affect the corneal epithelium, such as tetracaine (Pontocaine). Safety procedures which have been useful in preventing complications in other types of intraocular surgery, such as facial akinesia, retrobulbar injection with hyaluronidase, and speculums or retractors which do not press against the glove and superior rectus suture, will also serve the same purpose of preventing complications in corneal surgery.

Corneal surgery has become a very extensive subject, and therefore, in this limited presentation, I will have time to deal with the prevention of only the most important complications in keratectomies and keratoplasties.

Keratectomies.—Keratectomies are performed for corneal opacities either as a final treatment for visual purposes, if vision improves sufficiently with this procedure alone, or, as is often the case in densely vascularized leukomas, to improve the cornea structurally in order to be able to perform a keratoplasty under more favorable circumstances.

In keratectomies, while the external corneal lamellae are being dissected the cornea may perforate, in which case, if the dissection has been carried out carefully under a flap of corneal tissue, this flap may be used to cover the perforation. This corneal flap may be carefully sutured to the cornea surrounding the perforation in order to obtain a more accurate closure. The operation may then be postponed for several days or weeks until the anterior chamber has been re-formed, and either a similar or a different procedure can then be carried out. To anticipate this complication, if the cornea is suspected of being very thin and perforation is likely to occur during the dissection of the external lamella of the cornea, donor material for keratoplasty may be kept ready for use to proceed with either a partial or total lamellar corneal transplantation. If the deep layers of the cornea of the recipient are not found to be worth saving even for structural purposes, a different handling of the situation is to perform a total penetrating keratoplasty, which is generally the only procedure left to improve an eye under these circumstances.

The different types of keratectomies, with or without conjunctival plastic repair and buccal mucosa grafts, are too extensive to permit dealing with all or even the most important complications. Therefore, I shall proceed with a brief discussion of the prevention of complications in the rather extensive section on keratoplasties.

Keratoplasties.—Donor: The eye of the donor, if it is not enucleated aseptically, offers the greatest danger of carrying infection to the recipient's eye. Therefore, the eye of the donor must be obtained under aseptic conditions and preserved from contamination whether the eye is enucleated from a patient or from a cadaver.

In cadavers, it is advisable to enucleate the eye within 12 hours after death and to dissect the graft before the cornea begins to deteriorate and show maceration of the epithelium, edema, cloudiness, and wrinkling of Descemet's membrane. Usually the eyes may be preserved in a moist chamber at from 2 to 4 C for two to three days with a cornea which appears healthy and, therefore, fit for keratoplasty. It does not matter whether the eyes are enucleated from a patient or a cadaver of an adult or an infant or how long they have been preserved; as long as the cornea remains transparent it may be used to obtain the graft.

Although the epithelium of the graft will be completely regenerated by the host if it is missing, it is advisable to preserve it intact whenever possible in order to minimize the possibility of infection. A further precaution to prevent infection should be taken by irrigating the graft with a solution of penicillin and streptomycin before placing it in the eye of the recipient.

Recipient: When the eye of the recipient has received an overdose of irradiation, usually given to obliterate corneal vascularization, the graft shows a great delay in cicatrization, not infrequently developing fistulas leading to cloudiness,

opacification of the graft, or even the loss of the eye. These complications should be kept in mind and the dosage of irradiation preoperatively should be kept to a minimum.

The transplant may become opaque because the cornea was not suitable for a successful corneal transplant because of vascularization, symblepharon, etc. Therefore, the eyes should be rendered more favorable by preliminary surgery before keratoplasty is attempted. To prevent a poor result because the scar at the edge of the graft falls at or near the pupillary area, the graft should be adequately centered. In order to prevent injury to the iris or lens with trephines or knives, the instruments should be withdrawn from the cornea the moment the anterior chamber has been entered. Also to prevent injury to intraocular structures, manipulations within the eye must be carried out with scissors with blunt points and with toothless forceps.

In performing keratoplasties with large grafts, the lens may extrude. Adequate paralysis of the orbicularis, speculums or retractors which do not press against the eyeball, the addition of hyaluronidase for retrobulbar injection to reduce the tension of the eye, and pressure upon the eye before starting the operation, also to reduce tension, tend to prevent this complication. The incidence of extrusion or protrusion of the graft, development of fistula, hernia of the iris, and an anterior synechia will be greatly reduced if good apposition of the borders of the graft and cornea of the host is secured by direct suturing.

The sutures should not be removed before the 11th postoperative day. Complications at the time of the removal of sutures such as fistulation or complete extrusion of the graft should not take place if, at the time of removal of sutures, the patient has been adequately sedated, akinesia has been used, the orbicularis has been paralyzed, and adequate instruments are used. The use of gut sutures instead of silk would also prevent this complication but, on the other hand, gut material may be the cause of other complications, such as vascularization, formation of abscesses, and prolonged irritation of the eye.

High astigmatism and high errors of refraction are usually observed in keratoconus when the graft has not been large enough to remove the whole deformity. Therefore, in keratoconus, the graft should be large enough to remove the whole conical portion of the cornea to obtain a better curvature. If postoperatively the transplant has a tendency to protrude, irregular healing will take place, also with the development of high astigmatism and high errors of refraction. This protrusion can be treated postoperatively by the application of a pressure dressing from the third postoperative week until adequate curvature has been obtained.

Fuch's epithelial dystrophy will often recur over the graft unless the operation is performed at an early stage of the disease and with sufficiently large grafts to remove the whole area of diseased cornea. Postoperative vascularization of the graft can be handled by the administration of cortisone locally and, if necessary, systemically. If this treatment should fail, the vascularization may be stopped by β-radiation. In order to prevent delayed opacification of the graft, which usually begins in the third week postoperatively and which has been explained by some as a host-recipient sensitization and by others by the presence of foci of infection, all foci of infection should be removed preoperatively before performing corneal transplantation.

In lamellar grafts, to prevent vascularization at the base of cicatrization, bleeding blood vessels should be obliterated by electrocoagulation at the time of the operation and moderate pressure should be applied postoperatively to prevent the accumulation of exudates or blood under the graft.

In patients who may be allergic to certain medications, complications may be prevented if a careful history is taken preoperatively.

In total penetrating keratoplasty, postoperative glaucoma is frequently observed. This can be prevented by performing an iridectomy and lens extraction at the time of the operation and the administration of acetazoleamide (Diamox) during the postoperative recovery.

Glaucoma Surgery. PAUL A. CHANDLER, M. D., Boston.

The principal complications of iridectomy are injury to the lens and delayed reformation of the anterior chamber. If the incision is made with either knife or keratome, injury to the lens is a possibility, whereas the ab externo incision practically eliminates lens injury.

The lens can be injured with iris forceps. It is best to make the iris prolapse or present in the wound by separating the lips of the wound so that it can be grasped well peripheral to the lens. If forceps must be introduced into the eye, they must be smooth forceps, without teeth.

A flat anterior chamber not only defeats the purpose of iridectomy but may actually make the glaucoma much worse. If the incision is beveled, is kept small, and is tightly closed with sutures, one should never see a flat anterior chamber after iridectomy.

In the trephining operation the lens may be injured by the trephine blade. This can be avoided by deepening the anterior chamber with saline just prior to making the trephine opening. In iridencleisis and iridosclerectomy procedures unless the anterior chamber is deep there is risk of lens injury with knife or keratome. If the anterior chamber is shallow, the ab externo incision is safer. Only smooth forceps should be used on the iris.

Flat anterior chamber after filtering operations is undesirable from many standpoints. Meticulous closure of Tenon's capsule and the conjunctival wound will greatly lessen the incidence. A flat chamber can be reformed at any time by releasing subchoroidal fluid and injecting air into the anterior chamber.

Cataract Surgery. JOHN H. DUNNINGTON, M. D.

Inasmuch as most postoperative complications result from conditions arising before or during the operation, this discussion will be largely limited to the happenings in these periods.

Postoperative infection occurs about once in every one thousand cases. The value of preoperative cultures is debatable, and they are not used routinely. Select a clinically clean eye, and use an antibiotic (e. g., oxytetracycline) locally for 24 to 48 hours preoperatively. Routine systemic administration is not recommended either before or after operation.

Preoperative sedation should be adequate but not excessive. Individualization in the selection of the amount and kind of drug is essential.

Akinesia: O'Brien or Atkinson techniques are used. Additional injections along extraocular muscles when necessary are recommended.

Anesthesia: Retrobulbar injection of 2 cc. of 2% procaine hydrochloride plus five minutes of digital pressure, as advocated by Chandler and Atkinson, are routine measures.

Canthotomy is used whenever necessary to remove pressure of lids. A soft eye is our best safeguard against vitreous loss.

Incision should have complete conjunctival covering and be placed as far forward as possible. A bevelled incision from 10 to 2 o'clock is most desirable.

Corneoscleral sutures inserted either before or after incision should be appositional, should incorporate only a small amount of tissue, and should be tied lightly.

Opening in iris must be adequate to insure free exchange of aqueous between posterior and anterior chambers.

Delivery of lens: Intracapsulardelivery by tumbling technique is preferred. Careful inspection of forceps or erisophake is important. Grasp lens well behind iris in 6 o'clock meridian; lift it toward the cornea, and direct counterpressure toward table and patient's feet. As soon as dislocation occurs, change direction of pressure to plane parallel to that of anterior face of the vitreous and fold cornea behind the lens. Delivery should be slow, particularly when the sphincter of the iris is intact. Avoid excessive traction at terminal stage of delivery.

Management of rupture of capsule: If eye is soft, capsular remnants and cortex can be safely irrigated out or extracted with 2 pairs of Kalt type forceps,

with use of hand-over-hand technique. In any event, be certain that wound and upper part of anterior chamber are free of capsular and cortical remnants.

Management of loss of vitreous: If vitreous is viscid, complete iridectomy and sphincterotomy at 6 o'clock are recommended plus tight closure of wound with supplementary corneoscleral sutures.

Management of prolapse of iris: Prompt excision under ideal operative conditions—usually complete anesthesia—plus resuturing of wound is treatment of choice.

Retinal Detachment Surgery. CHARLES A. PERERA, M. D.

The discussion of this subject will be limited to the complications occurring during the operation, those caused by the surgical procedure, and the factors which play a part in failure to reattach the separated retina. These three groupings cannot be sharply separated from each other.

Hemorrhage.—Retrobulbar hemorrhage resulting from injection of procaine into the orbit is rare. It can be prevented by careful technique and the use of a fine gauge needle with a rounded point.

The incidence of choroidal, retinal, and vitreous hemorrhage can be much reduced by care in avoiding the vortex veins and their ampullas and the long ciliary vessels and by the use of short diathermy needles so as to limit the intended reaction to the sclera and choroid. Great caution must be used in evacuation of subretinal fluid and vitreous by the use of longer needles, the enlargement of a needle opening by a punctum dilator, or the performance of an incision with a cataract knife. The drainage sites should be situated within an area which has been previously treated with coagulating diathermy.

Infection.—Intraocular infection following operation for retinal separation is exceedingly rare. A stubborn chronic conjunctivitis, usually bilateral, occurs occasionally as a result of bandaging and closure of the eyes before and after surgery. Both intraocular and extraocular infections can be largely prevented by careful attention to asepsis and the use of rubber gloves during the operation and by the employment of antibacterial agents in the conjunctival sacs before and after the surgical procedure, avoiding those to which the patient is sensitive. Allergic reactions of the eyelids and conjunctiva may follow the use of mydriatics and antibiotics.

Tissue Reaction.—Postoperative tissue reaction may result from the presence of cotton fibers, from careless closure of the incision through the conjunctiva and Tenon's capsule, and from tearing of the conjunctiva. Since careful drying of the sclera is important in using the coagulating current, sponging with moist cotton or gauze sponges or with other types of sponges should be accomplished by gentle pressure, not by rubbing.

The incision through the conjunctiva and Tenon's capsule should be made at least 7 or 8 mm. behind the limbus, and both layers should be closed with a single line of interrupted sutures at the end of the operation. Care in handling tissues during operation will prevent torn and ragged edges and excessive postoperative scars.

Overtreatment with the diathermy current may result in postoperative vitreous bands and contracting fibrous tissue within the retina or on its surface. On rare occasions, shrinkage and atrophy of the globe may follow overtreatment. The diathermy current used for coagulation should be just sufficient to cause slight shrinkage and darkening of the sclera when this layer is touched. Overtreatment may also cause chorioretinal changes at some distance from the site of the application, sometimes along retinal vessels. In one patient, with traumatic separation of the retina after boxing, application of the treatment at the superior equator of the eyeball resulted in a chorioretinal scar above the macula. In this case, luckily, the vision of the injured eye is still 20/20 six years after operation.

Overtreatment may cause overheating of the intraocular tissues. Cooling by irrigation after each diathermic application may be effective if the intensity of the current cannot be reduced.

In surrounding the site of a retinal tear with two or more circles of diathermic applications, the intensity of current should be reduced the farther the treatment areas are placed from the location of the hole, so as to avoid the formation of traction bands and new retinal tears.

In the operation employing lamellar resection of the sclera, the floor of the scleral trench may be touched with surface applications of the coagulating current or with a small sponge moistened with 2% or 3% solution of potassium hydroxide. In using the chemical solution, the scleral walls should be avoided and the applications should be followed immediately by thorough irrigation with saline or weak acetic acid solution. In 2 of the last 50 lamellar resections of the sclera which I have performed, there was a considerable cloudiness of the vitreous during the week after the operation, causing me to suspect early intraocular infection. In both cases, the vitreous gradually cleared and the retina remained reattached. In both patients I employed antibiotic therapy by the systemic and local routes.

Prolapse of choroid with possible accompaniment of vitreous and retina is a complication of the excision of a strip of the entire thickness of the sclera. This untoward accident can be prevented by preplacement of the scleral sutures and progressive tying of the sutures as the scleral strip is excised or by the much preferred performance of lamellar resection of the sclera. In the latter procedure, the thin inner layer of remaining sclera allows the surgeon to proceed with subsequent suturing, avoiding choroidal prolapse from slight pressure on the globe or from the distorting effects of traction sutures.

Accidental perforation of the sclera in areas of necrosis from a previous operation can be avoided by care in dissection and treatment.

Difficulty in bringing together the edges of the sclera when a lamellar resection is performed can be avoided when the globe is not soft by excising a strip not wider than 3 or 4 mm. and by evacuating subretinal fluid and aqueous if necessary.

Oculomotor Anomalies.—Vertical and horizontal muscle anomalies are seen occasionally after surgery for retinal separation. This complication will happen only rarely if the muscles are handled with care and if Tenon's capsule and the muscle sheaths are not damaged by the diathermic current and mechanical trauma. It is rarely necessary to detach a muscle in performing the diathermy operation except when the posterior pole of the eyeball requires treatment. The Arruga speculum or some similar instrument, with appropriate traction sutures, permits good exposure of the operative field. It is easy to pull the muscle to one side and treat the sclera beneath it.

In scleral resection operations, a muscle or two must usually be temporarily detached. In a few patients there is a postoperative overaction in the field of the detached muscle, probably the result of contraction of scar tissue. In my experience, postoperative diplopia from this cause is rare, and then it most often is a sequel of operations following a first unsuccessful procedure.

Complications from Intravitreal Injections.—The injection of air, saline, or vitreous into the vitreous cavity at the close of the operation, unless performed through the posterior pars plana of the ciliary body with the needle directed toward the center of the globe, may cause further retinal detachment, traumatic cataract, or rupture of the eyeball at a point in the sclera weakened by a previous diathermy operation or scleral ectasia. The means of prevention of these accidents are obvious.

Failure to Reattach the Retina.—This outcome might be considered as a complication of retinal detachment surgery. I shall only enumerate the main causes of failure, the incidence of which can be reduced by careful and prolonged preoperative study of both eyes and attention to the technical details of the surgical procedure: (1) failure to close original tear or tears, (2) failure to find one or more tears initially, (3) the development of new tears after operation, (4) failure to find any tears, (5) shrinkage of the retina, (6) presence of contracting vitreous strands, (7) failure to evacuate subretinal fluid and subretinal

vitreous and failure to provide adequate drainage of these if the retina is not in place at the end of the operation.

Eye Muscle Surgery. RAYMOND N. BERKE, M. D.

The prevention of major complications following extraocular muscle surgery is of paramount importance to every ophthalmologist.

Fortunately, most of these complications can be prevented by careful and judicious technique. For example, when doing a myectomy of the inferior oblique at its origin, accidental tenotomy of the inferior rectus can always be prevented by executing the "traction test" on the inferior oblique muscle. This test is performed as follows: After incision of the conjunctiva of the lower fornix and delivery of the inferior oblique into the wound, the speculum is removed. The surgeon then palpates the lower nasal quadrant of the orbit through the skin of the lower lid while making traction on the squint hook. If the inferior oblique has been engaged on the hook, the surgeon will feel a cord-like band of tissue extending from the shank of the hook toward the site of origin of the inferior oblique muscle. If this test is positive, one can be sure that the inferior oblique and not the inferior rectus is on the hook. Myectomy of the inferior oblique can then be done without fear of injuring the inferior rectus.

The inferior oblique muscle may be accidently severed while the lateral rectus muscle is being resected. This complication occurs because the sheaths of the inferior oblique and the lateral rectus blend together with Tenon's capsule, so that when the squint hook is passed under the lateral rectus from below, the inferior oblique is pulled forward on the hook. If this situation is not rectified, the displaced inferior oblique will be injured while the lateral rectus is being freed from Tenon's capsule. This complication can always be avoided by passing a second squint hook under the lateral rectus from above (thus disengaging the inferior oblique and allowing it to fall back to its normal position) before freeing Tenon's capsule from the lateral rectus muscle.

The reflected tendon of the superior oblique may be accidently severed while the superior rectus muscle is being resected. This complication occurs because the superior oblique tendon lies close to the insertion of the superior rectus and because the sheaths of these two muscles blend together at this point. Thus, the tendon of the superior oblique may be caught on the squint hook inserted under the superior rectus and be injured when the superior rectus is freed from Tenon's capsule. This complication can always be prevented by executing the "traction test" on the superior oblique before freeing the superior rectus from Tenon's capsule. If one can feel a cord-like band of tissue through the skin of the upper lid extending from the pulley of the superior oblique to the squint hook under the superior rectus, one can be sure the reflected tendon of the superior oblique or its sheath is engaged on the hook. If a second hook is passed under the superior rectus, the reflected tendon will be disengaged so that the superior rectus may be freed from Tenon's capsule without fear of injuring the superior oblique tendon.

Operations on the medial rectus muscle seldom produce serious complications. However, one major complication should be mentioned, namely, accidental perforation of the sclera. This dreadful complication may occur while any extraocular muscle is being freed from the sclera, but it is most likely to occur in strabismus fixus. It can be avoided by cutting the tendon from the globe by means of a canaliculus knife, as suggested by Brown, or by taking short snips with the points of the tenotomy scissors directed away from the sclera.

Thus, all of the major complications mentioned here can be prevented by careful and judicious technique.

Discussion

DR. JOHN M. MCLEAN: I have been asked in just a few minutes to discuss the presentations of the first three speakers on this symposium and to add a word or two about Dr. Jaffe's interesting presentation. I shall be very brief. We can say about all of these presentations many things in general, because all of them

are operations which involve opening the anterior segment of the eye. Adequate akinesia, anesthesia, sedation, and so forth, have all been discussed. I should like to add, to that segment of our topic concerning the preparation of the patient to avoid complications, the instillation and maintenance of the patient's confidence, which I think is terribly important, both before, during, and after the operation. In that connection, one thing which I like to stress above all is avoidance of indication to the patient during the operation that something may be amiss, whether it is or is not. Angry or profane exclamations—not because they are profane, but because they immediately let the patient, who is awake, know something is not the way you like to have it—bawling out the assistant, or calling down the nurse should all be avoided. Say as many unkind things as you like when the patient is out of the room, but doing it in front of the patient is inviting, instead of preventing complications. Too dramatic calls to the nurse or assistant for "knife" or, worse than a knife, for "cautery!" are enough to scare any patient whose eye is under operation. This type of dramatics may have its place on the legitimate stage, but it has none in the operating theater. One complication—so many have been mentioned tonight—but one I think that has not been mentioned, that is on the increase more than any other, may be invited by remarks in front of the patient. That complication is the malpractice suit, which can be prevented, at least in part, by being a little more careful about what you say in the patient's presence.

Now to be a little more specific about Dr. Jaffe's interesting presentation and methods, I, too, have used this technique almost exactly as he describes it, with a few minor modifications, for some years and have found it very satisfactory. I know he uses preplaced sutures, and when the eye is as soft as he likes to have it, and as I like to have it, I think preplaced sutures are very helpful in getting proper alignment of the section and preventing poor wound closure. With as soft an eye and as collapsible an eye as we are aiming for, if you try to locate them after the incision is completed your alignment may not be so good. Also, this type of softened eye enables you to open the wound at the end of the operation and inspect it carefully, directly, under magnification, to allow the iris to fall back with safety, instead of poking around with iris repositors, in an attempt to get a clean incision and avoid incarcerations.

The presentation on corneal surgery leaves very little that I can add to. I should like to ask Dr. Castroviejo two questions. I wonder why he is still so opposed to chromic gut sutures for corneal surgery. I was opposed to them, too, for some time, but in the last couple of years have been using them with increasing frequency, starting out with alternating silk-gut, silk-gut sutures around the edge of the transplant, and found to my surprise that the chromic sutures seemed to be just as satisfactory, or sometimes more satisfactory, and recently I have used them extensively.

The second question is why he insists on taking the silk sutures out by the 11th day. Why not wait a little longer? They don't seem to do any harm if they stay in for three weeks, and there is less chance for complication in suture removal. I was interested in looking back over an old symposium in which Dr. Castroviejo and I both participated. In it we both stated that direct sutures could not be used in corneal transplants because there was too much trauma to the transplant, and in those days they could not, but the improvement in sutures and needle material has made it possible, with a marked reduction in complications.

If Dr. Chandler will have a chance to say a few more words I should like to ask him to say one thing which I know he can say very emphatically, something on which he and I agree completely. I think he would like an opportunity to say a few words about the dangers of acetazoleamide in certain situations in angle closure glaucoma, and I think that should be mentioned in connection with the prevention of complications.

Finally, Dr. Dunnington has covered so fully the prevention of complications in cataract surgery he has left me very little to say. I would remind you again of one thing we have all talked about many times which I do not think he mentioned, though I know he considers it, and that is the importance of having respect for

the endothelium of the cornea during manipulation inside the chamber in the course of cataract extraction.

In connection with what he said about removing the capsule and cortex—perhaps it is a peculiarity of mine, but I do find adequate ultraviolet illumination a big aid in removal of the lens which remains at the end of cataract operation.

Unlike Dr. Dunnington, who said that all his extractions—he said it with a smile—were either planned intracapsular or planned extracapsular, I can still say with a smile, but seriously, that all mine are either planned intracapsulars or extracapsulars which are a complication and not intended that way.

In connection with all of these presentations, perhaps they should be summed up by saying that complications are best avoided by foreseeing them before they arise, by adapting the techniques to fit the individual situation, and by considering the over-all needs of the patient rather than trying to fit him into some stereotyped, preconceived surgical pattern.

DR. RAYMOND E. MEEK: Dr. Perera and Dr. Berke are both surgeons for whom I hold the greatest respect, and I am, in general, in complete agreement with the complications outlined by them. In my following comments I may reiterate statements made by them, but I do so only for emphasis.

As Nature abhors a vacuum, I believe that an eye if properly treated must return to normal and the retina will always reattach itself if the surgeon is able to restore conditions whereby the retina can reattach itself and the tears are sealed.

Diathermy alone cures 60% to 70% of cases of retinal separation, according to Seymour Phelps, but this is not enough. Therefore, in certain cases we must resort to some method of shortening the eyeball. Also it may prove necessary to inject air, saline, or vitreous, to restore the retina to its position of resting on the choroid and hold it there until healing takes place. In cases where the retina cannot be made to fit the eye, the eye must be shortened to fit the retina.

In my opinion, many cases of scleral shortening operations are apt to fail unless the retina is shortened in two directions, not only from behind forward but also from side to side. In stretching a curtain, if the side boards are supported and the end board is removed, the curtain—representing the sclera—will retract in folds, but the folds are still on the stretch from side to side and then one of the side boards must be released. With this fact in mind, I devised the meridional lamellar scleral resection so that the sclera is shortened not only from before backwards but also from side to side. The results with this advance in technique have been highly satisfactory.

Although Dr. Perera has almost never or never had postoperative hemorrhage, I feel that the reason some of us have seen this complication is because proper care has not been taken to avoid the long posterior ciliary arteries and the venae vorticosae. Even without hemorrhage, destruction of the long posterior arteries may cause anterior choroiditis and postoperative cataract.

In the short time alloted to the speakers it is impossible to cover all complications in muscle surgery, but Dr. Berke has ably covered the most important ones. I would like to emphasize a careful observation before surgery to rule out a paralyzed muscle. Careful measurement is necessary, because if a muscle is severed 3 mm. from its insertion in the sclera and then the cut end is placed 4 mm. behind the insertion one may get a recession of only 1.0 mm. as a final result.

I should like to reiterate my old saying in all surgery: A great many complications of a serious nature can be avoided if we always ask ourselves: Am I operating on the proper patient? Am I operating on the proper eye, and am I doing the proper procedure?

DR. RAMON CASTROVIEJO: I should like to thank Dr. McLean for his kind discussion. When I mentioned the 11th day as the best time for the removal of the sutures, I meant that as the earliest time that they should be removed. They may be removed later than the 11th day if the eye does not show any unusual irritation. If they are left longer, abscesses may be formed and the eye may show more prolonged postoperative reaction. This irritation generally increases in larger grafts where the border approaches the limbus. Gut material sometimes takes

three or four weeks to reabsorb, unnecessarily prolonging irritation of the eye and encouraging vascularization of the cornea of the host and sometimes of the graft and the development of abscesses. The more chromic the gut, the longer it takes to reabsorb.

DR. PAUL CHANDLER: The matter of acetazoleamide is not exactly an operative complication, but its ill-advised use, I think, can lead to situations where all operations fail, and then it may be said to lead to a complication; so perhaps its use should be mentioned here. First of all, let me say that in open angle glaucoma I see no contraindication to the free use of acetazoleamide, as much as the patient tolerates. In angle closure glaucoma, however, both acute and subacute types, it is my feeling that it should be used exclusively as an immediate preoperative measure—in other words, when the patient is in the hospital and you are preparing for operation. If it is used as a therapeutic agent outside the hospital, along with miotics, owing to the fact that it lessens the production of aqueous, it has a pressure-lowering effect, and the pressure is no longer a guide to the state of the angle of the anterior chamber. Without acetazoleamide, if miotics are used, if the pressure is 60 and comes down to normal that is positive proof that the angle has almost completely opened; therefore this is a favorable case for simple iridectomy, even if it has been neglected. If, on the other hand, with miotics alone, the pressure will not come lower than 40 or 50, one can be certain that a large portion of the angle is closed, and one must plan the operative procedure accordingly. However, if in this patient acetazoleamide is used while the patient is still being treated outside the hospital, a tension of 60 may be brought rapidly to 30 or 25, but all the time a considerable portion of the angle may remain closed. If this treatment is continued, more and more permanent peripheral synechias may form, and as a result of the delay all chance of cure with a simple iridectomy is lost. You are all familiar with the difficulties in treating patients who have extensive peripheral synechias. Iridectomy won't cure them; many times filtering procedures fail, and some of those eyes are lost which could have been saved if they had been operated upon immediately without being treated for a long time with acetazoleamide, thereby allowing permanent closure of a large part of the angle. Therefore, I should like to reiterate my opinion that acetazoleamide has no place in the treatment of angle closure glaucoma, acute or subacute, except as an immediate preoperative measure.

DR. JOHN H. DUNNINGTON: There really is very little excuse for me to get up again except to thank Dr. McLean for emphasizing the value of keeping quiet during an operation. I probably do not think about it, because, as some of you know, my preceptor (Dr. John M. Wheeler) was known for not saying much and I have always followed this teaching. Usually I never comment during a routine cataract extraction, but I once made the remark to my assistant, "Shall we close this with a running suture?" and the patient heard the word "running," and, as Dr. McLean said, it took a lot of talking to restore confidence. Therefore, I want to reiterate that the operating table is no place for loose talk, and I am so delighted that Dr. McLean brought it up.

DR. CHARLES A. PERERA: I want to correct Dr. Meek's impression; I have seen hemorrhages both in my own cases and in those of others.

I think in eliminating complications from surgery of all kinds it is a good idea for us to theorize, and I think that the theory of Raymond Meek in shortening the eye in two planes is a very good one. I think the operation in his hands has proved to be a very worth-while and commendable effort. If more of us did this procedure we would be able to evaluate it. In theory at least, and probably in practice, too, if the eyeball can be shortened in two directions, the result will be more satisfactory. A great deal of advance has been made in nuclear physics and in other fields by sitting in a chair and thinking, and sometimes the theories we evolve in that way have real value.

It has been interesting to me to hear these very interesting talks, and I wish to thank Dr. Meek for his discussion.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

I. S. Tassman, M.D., Chairman
William E. Krewson, 3rd, M.D., Clerk
Oct. 25, 1956

Carcinoma of the Lacrimal Sac. EDMUND B. SPAETH, M. D.

This case is reported in full on page 689 of the May issue of the ARCHIVES.

The Use of Chlorpromazine in Cataract Surgery (Preliminary Report). R. D. HARLEY, M. D., and J. E. MISHLER, M. D. (both by invitation).

Nausea and vomiting during the operative or postoperative period in intraocular surgery are symptoms which have caused considerable concern to the ophthalmic surgeon. These symptoms may lead to serious sequelae, and any drug or method which might reduce these complications should be most helpful. Furthermore, in ophthalmic surgery in which operations are frequently performed under local anesthesia, there has been a need for an effective adjuvant to tranquilize the patient. Chlorpromazine was chosen for this study because of its reputed ability to relieve anxiety and reduce the incidence of nausea and vomiting.

An attempt has been made to evaluate the usefulness of chlorpromazine (Thorazine) in 100 consecutive cataract extractions. The results have been compared with a previous series of 100 consecutive cataract extractions in which chlorpromazine was not used.

The first 100 consecutive cataract extractions had the following preoperative routine: sodium pentobarbital 100 mg. the evening preceding surgery; nothing by mouth four hours preoperatively; sodium pentobarbital 100 mg. four hours preoperatively and sodium pentobarbital 100 mg. one hour preoperatively, and meperidine hydrochloride 50 to 100 mg., according to weight and age, and dimenhydrinate 50 mg. one-half hour preoperatively. Postoperatively meperdine hydrochloride 50 mg. every four hours as required for pain or acetylsalicylic acid 600 mg. was given.

The second 100 consecutive cataract extractions had the identical preoperative orders with the addition of chlorpromazine hydrochloride 25 mg. orally one-half hour preoperatively. Chlorpromazine hydrochloride 25 mg. was given parenterally immediately postoperatively and again every three hours for nausea or vomiting as required.

The tranquilizing and calming effect of chlorpromazine has an impressive therapeutic effect on apprehensive, tense, and anxious patients. This unique quality of the drug is of tremendous value for the surgeon and patient alike in the operating room and during the immediate postoperative period. This fact does not reveal itself readily in figures, but by clinical observation one may conclude that there was at least a 10% improvement in the alleviation of anxiety and apprehension.

The act of vomiting allows one to be much more objective about the recording of figures. Nausea and vomiting were further subdivided into minimal and severe. Minimal nausea or vomiting occurred once or twice, while the severe form occurred three times or more. It becomes evident that the severe form of vomiting is of primary concern and the major symptom to be watched for and reduced to a minimum.

Statistical analysis of these results indicates that the number of cases is sufficiently large (100 cases with chlorpromazine and 100 cases without chlorpromazine) to reach or exceed the 5% level of probability by the χ-square technique.

Chlorpromazine seemed to have little effect on minimal nausea and vomiting in our series. It appears most useful in severe nausea and vomiting. Further investigation may show that an improved dosage technique will further reduce nausea and vomiting. Such a new series is in progress.

Discussion

DR. J. E. MISHLER: I should like to add a few remarks regarding the hypertensive effect. The drug chlorpromazine should not be given to those patients who have hypertensive cardiovascular disease.

With chlorpromazine preoperatively the patient came to the operating room relaxed, and in a dozing manner, but could be easily awakened. There were several cases which developed too narcotized a condition owing to the potentiating effect of chlorpromazine on the meperidine; with the help of oxygen for about 15 minutes these patients recovered to a wakeful state where we could continue the operation.

Many of the patients developed the gray, or chlorpromazine, look about which you have just been told, but in the beginning it was difficult to distinguish between the chlorpromazine "look" and clinical shock. Later we discovered that the pulse was strong in these cases, respirations were not labored, and, although it was lower the blood pressure did not drop as much as in clinical shock; furthermore, the skin itself, even though gray, was warm and dry.

We had no complications of jaundice in our series, although I understand a few cases have been reported. For one week up to six months, the percentage of jaundice was about 1% or less, but in our cases we did not find that. The jaundice is supposed to be a form of allergy, because it disappears on the withdrawal of the drug, and also patients with known cirrhosis of the liver or liver damage did not become jaundiced on chlorpromazine. The intramuscular injection is painful, but procaine hydrochloride 2% injected in the same area can relieve the pain. The subcutaneous and intravenous routes are definitely not to be used. Chlorpromazine solution has been known to cause a contact dermatitis in nurses who handle the drug frequently. However, we noticed no cases of contact dermatitis in our series.

Report of a New Carbonic Anhydrase Inhibitor (Squibb MC-9367). LT. MARVIN H. HALISTOCKY (MC), U. S. N. R. (by invitation), and BERNARD C. GETTES, M. D.

Single oral doses of 500 mg. of propanyl derivative of acetazoleamide (Diamox) known as Squibb N (5-sulfamoyl-1, 3, 4-thiadiazole-2YL) propionamide, or MC-9367, lowered the intraocular pressure 6 mm. of mercury or more (Schiøtz), in 18 of 40 normal eyes of 23 control patients at the Philadelphia General Hospital Blockley Division. Reduction in tension occurred in a total of 39 eyes of this group.

Thirty patients with narrow, wide, and secondary types of glaucoma, who required acetazoleamide for control of tension, were observed after the acetazoleamide had been withheld. Significantly, lower tensions resulted in 13 out of 13 eyes of 9 patients with narrow angle glaucoma, in 16 out of 19 eyes of 11 patients with wide angle glaucoma, and in 8 out of 11 eyes of 10 patients with some form of secondary glaucoma.

The greatest effect was noted two to four hours after the administration of the drug, and in the tension of patients with glaucoma. No paresthesia or any other toxic effects were noted after giving a single dose.

The effect of MC-9367 appears to be similar to that of acetazoleamide.

Discussion

DR. BERNARD GETTES: Whenever a new drug is reported, we immediately expect to hear of some dramatic development. As you have gathered from the presented data, this product offers nothing spectacular. It is similar in action to acetazoleamide; it is neither better nor worse.

The question arises, then, as to why this drug was investigated. The Squibb Institute for Research reported that there was a greater amount of excretion of body fluid with MC-9367 than with acetazoleamide. With this in mind, we felt that perhaps this agent would be effective in patients who at first responded to

acetazoleamide but later developed a resistance. We also considered that the additive effect might be better than with either agent used singly. We had hoped to study this product at greater length, but we found that experiments with use of this drug in cardiac conditions were being made simultaneously with our work. We did not use multiple doses, since there was no record of the toxic effects, and the manufacturer informed us that other investigators had encountered unfavorable effects and that they were, therefore, discontinuing the manufacture of this preparation.

Further investigation has been discontinued on the advice of the manufacturer. "Please do not use this drug. It becomes toxic if given over a prolonged period." What the unfavorable symptoms are, we are unable to report, since these data were not made available to us.

In conclusion, we have here another heterocyclic sulfonomide derivative, one of a group of compounds that were found, in 1950, to be carbonic anhydrase inhibitors. This preparation, MC-9367, after a single dose, has precisely the same degree of effectivity as acetazoleamide in lowering the intraocular tension in humans.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Nov. 15, 1956

The Nineteenth Annual Lecture in Honor of the Late Dr. George E. De Schweinitz: Central Serous Choroidosis Associated with Amebiasis; A Record of Nine Cases. ALSON E. BRALEY, M.D., and HENRY E. HAMILTON, M.D. (Delivered by Dr. Braley).

The gradual loss of central vision is disastrous to the patient and when associated with a central choroidosis or retinitis is commonly progressive and fails to respond to treatment, resulting ultimately in a central scotoma. The cause is ordinarily unknown. This paper reports nine patients who were found to have a central or macular lesion and also evidence of amebiasis. When treated properly for amebiasis, progression of the central lesion was stopped and healing took place. The patients under consideration came to the ophthalmologists because of loss of vision and were found to have a macular lesion.

The patients were studied carefully for evidence of tuberculosis, syphilis, brucellosis histoplasmosis, lupus erythematosus, diabetes, lymphoma, malaria, and other associated diseases by appropriate laboratory tests and observation of the clinical course.

All cases were found to have good clinical evidence compatible with active amebiasis. This, I think, may be important in the pathogenesis of the eye lesion. Six patients had stools positive for Endamoeba histolytica. The other three, however, had varied histories with bowel symptoms, were chronically ill, had enlarged tender livers, coppery color of the skin, and colitis by sigmoidoscope, and all had a positive compliment-fixation test, which became negative with treatment.

The clinical illness of amebiasis responded to therapy with eventual recovery following repeated courses of combined treatment with diiodohydroxyquin (Diodoquin), chloroquine, and/or carbarsone. After we had established a diagnosis of amebiasis, antibiotics were not used.

The following points concerning the clinical course of the eye lesion will be made. These cystic pigmented hemorrhagic lesions progressed unabated when the patients had been treated previously with typhoid vaccine, antibiotics, chlortetracycline (Aureomycin), oxytetracycline (Terramycin), streptomycin, penicillin, and also histamine. They were made worse with corticotropin and/or cortisone. It was also noted that between early courses of treatment with more specific

antiamebic drugs some progression was occasionally noted, but also that this progression appeared to be coincident with recurrent symptoms of clinical amebiasis. With multiple courses of antiamebic drugs, the lesion became quiescent in a few weeks to a few months and healed. The patients had been followed from over one to seven years. The lesions were bilateral in four and unilateral in five cases. The amebic infection was thought to antidate the eye lesion ordinarily by one to several years.

Summary: Nine patients are presented with lesions of the macula characterized by cystic elevation, hemorrhage, and pigment, and also each patient had evidence compatible with active amebiasis.

The treatment with multiple courses of antiamebic drugs resulted in healing of macular lesions and arrest of the visual loss, with occasional improvement of vision.

The lesion was made worse with corticotropin and cortisone.

It is suggested that all patients presenting with a macular lesion of obscure etiology be studied for evidence of amebiasis.

News and Comment

ANNOUNCEMENTS

Pennsylvania Academy of Ophthalmology and Otolaryngology.—The fifteenth annual meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology will be held May 23-25, 1957, at the Bedford Springs Hotel, Bedford, Pa. Dr. Chevalier L. Jackson, President of the Academy, will preside. The guest of honor for the meeting will be Dr. Edwin N. Broyles, of Baltimore.

The meeting will consist of study clubs and general sessions. The faculty for the study clubs will be members of the societies. The general sessions will be given by members of the societies and also invited guests. Those invited to participate are the following:

Ophthalmology

Philip M. Lewis, Professor and Head of Department of Ophthalmology, University of Tennessee, Memphis

Lorenz E Zimmerman, Chief, Ophthalmic Pathology Section, Armed Forces Institute of Pathology; Physician Specialist, Central Laboratory, Veterans Administration, Washington, D. C.

Harry S. Weaver Jr., Professor and Head of Department of Ophthalmology, Hahnemann Medical College and Hospital, Philadelphia

Roscoe J. Kennedy, Head of the Department of Ophthalmology, Cleveland Clinic Foundation, Cleveland

Richard E. Hoover, Baltimore

G. Victor Simpson, Surgeon (Ophthalmology) and Chairman of Dept. of Ophthalmology, Episcopal Eye, Ear and Throat Hospital; Consultant in Ophthalmology, Walter Reed Army Hospital, Washington, D. C.

John M. McLean, Director, Department of Ophthalmology, New York Hospital; Consulting Ophthalmologist, New York Eye & Ear Infirmary

Otolaryngology

Robert L. Goodale, Assistant Clinical Professor of Laryngology, Harvard Medical School; Consulting Surgeon (Otolaryngology), Massachusetts Eye & Ear Infirmary, Boston.

Harry C. Rosenberger, Chief of Department of Otolaryngology, St. Luke's Hospital; Consultant in Otolaryngology, Women's Hospital and Huron Road Hospital, Cleveland

Maxwell Ellis, London, England

A symposium on the doctor and insurance will be held one evening. Three members of the Academy; George Hafer, Attorney for Blue Shield, and Robert Shinn, Vice President, Medical Insurance Company, will participate.

A symposium on the practical management of the child with a hearing problem, with announcement of the new State program, will be held Thursday afternoon. This year, except for Thursday afternoon, all sessions will be held from 9 a.m. to 1 p.m., allowing the afternoon for recreation.

International Organization Against Trachoma.—The next meeting of the International Organization Against Trachoma will be a one-day meeting during the meeting of the XVIII International Congress of Ophthalmology, which will be held in September, 1958, in Brussels, Belgium. The exact day has not been decided upon.

International Association for Prevention of Blindn ss.—A Congress of the International Association for the Prevention of Blindness will be held during the meeting of the XVIII International Congress of Ophthalmology, in September, 1958, in Brussels, Belgium.

PERSONAL

Prof. Alan C. Woods.—Prof. Alan C. Woods, of the Wilmer Institute, was a guest speaker at several Latin American medical schools during February, 1957.

Invited by the Escola Paulista de Medicina, Dr. Woods gave five lectures on uveitis in São Paulo, which were attended by a large number of ophthalmologists from all over Brazil. In Montevideo, Dr. Woods was the guest of the Medical College of the University of Montevideo, and in Buenos Aires he was the guest of the Medical College of the University of Buenos Aires. Dr. Woods also lectured in Santiago and was invited by the University of San Marcos de Lima to lecture there.

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*Schlegel, H.E.,Jr., and Swan, K.C.: A.M.A. Arch. Ophth. *61*:663 (May) 1954. Emmerich, R.; Carter, G.Z., and Berens, C.: An Experimental Clinical Evaluation of Dorsacaine Hydrochloride (Benoxinate, Novesine), report on the instillation of a 0.4 per cent solution, Am. J. Ophth. *40*:841 (Dec.) 1955. Fasanella, R. M.: Glaucoma in General Medical Practice, Connecticut M.J. *20*:282 (April) 1956.

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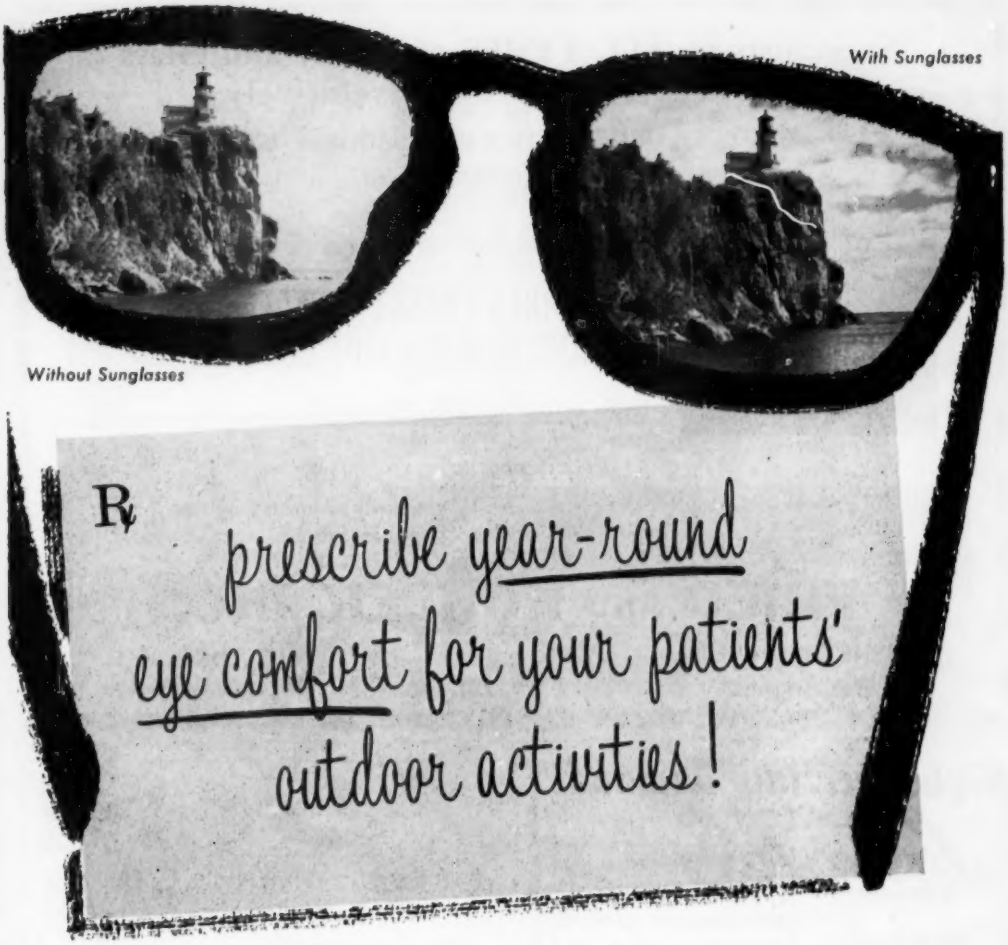

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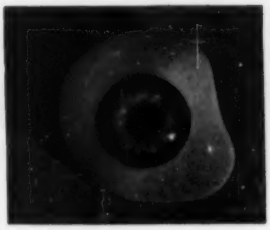

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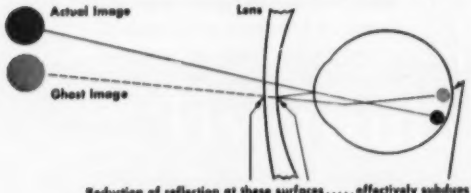

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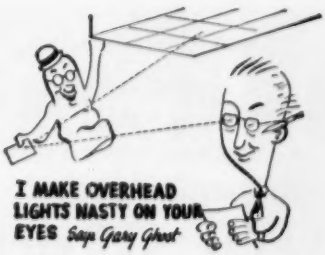

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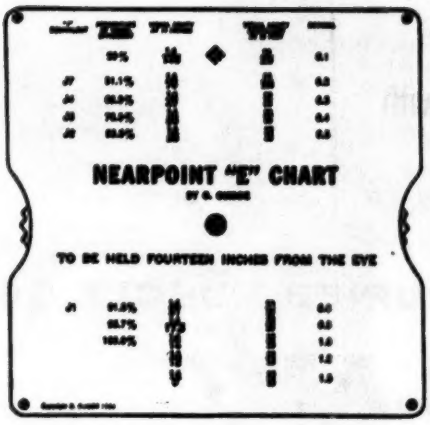

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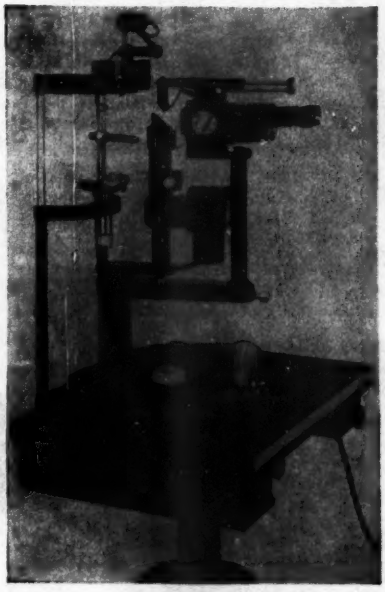

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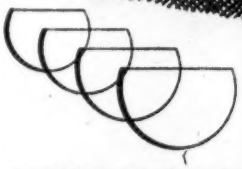

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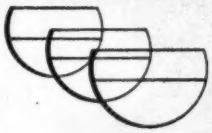

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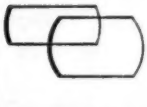

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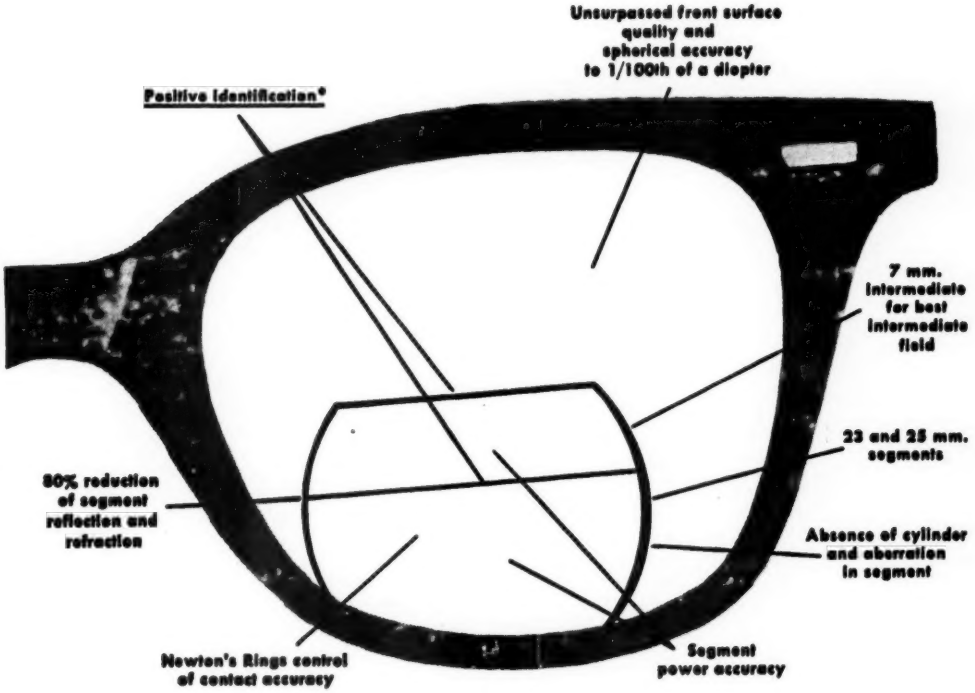
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